

## **Abstracts**

### **Talks**

#### **Session A: Cellular Systems**

##### **A-01 Kris N. Dahl, Carnegie Mellon University**

###### ***Nuclear structural changes with aging***

*The structural proteins of the nucleus primarily reside at the nuclear envelope and are responsible for maintaining mechanical nuclear integrity. Nuclear intermediate filament lamins A, B and C form the nuclear lamina network stabilized by many lamin binding proteins. Both mechanical stability and mechano-sensitive gene expression are altered in cells with mutations in lamin proteins, including Hutchinson-Gilford progeria syndrome (HGPS). We study the structure, self-assembly and mechanical changes in HGPS at many length scales - molecular, multi-molecular, network, nuclear, cellular and multi-cellular - using biophysical and computational approaches. In HGPS, a mutant form of lamin A, also called progerin, causes lamin accumulation at the nuclear membrane resulting in structural and mechanical anomalies. We use purified protein fragments of lamin A and progerin to quantify changes in molecular protein stability in the cell. At the cell level, we use micromanipulation to quantify the viscoelastic properties of isolated nuclei from human fibroblasts from HGPS patients and in model cell systems which exogenously overexpress progerin. Nuclei from HGPS patients show significant quantitative reduction in the ability to rearrange, and the HGPS nuclei collapse along major axes, suggesting catastrophic failure to distribute applied forces across the entire lamina. In multicellular systems exposed to shear stress, we have shown that nuclei in cells expressing progerin are unable to respond to force as control nuclei do by global reorientation in response to flow and by subnuclear force-mediated reorganization possibly related to mechanotransduction. Thus, we see how changes in redistribution of individual proteins can lead to mechanical changes in the nucleus and further alter cellular response to flow in a multicellular system.*

##### **A-02 Helim Aranda-Espinoza, University of Maryland With Kimberly M. Stroka**

###### ***Leukocyte transmigration tailoring substrate mechanical properties***

*Cardiovascular disease (CVD) is the leading cause of death in the world. One type of CVD, atherosclerosis, occurs due to an over-accumulation of leukocytes which adhere to the vascular wall, transmigrate through the endothelium, take up lipid particles, and form plaques causing obstruction to blood flow. This process leads to an overall stiffening of the arteries and often heart attack or stroke. It is understood that in addition to biological signaling events, physical force propagation through endothelial cells (ECs) is crucial in regulating the health of the vasculature; thus, it is important to study the biophysical aspects of ECs during leukocyte transmigration. In this study we used polyacrylamide (PA) gels of varying stiffness with extracellular matrix proteins incorporated to mimic the basement membrane, plate human umbilical vein ECs (HU-*

VECs) onto the surface of the substrates, and allow them to form monolayers. We observe that substrate mechanical properties affect the morphology, cytoskeletal arrangement, and stiffness of HUVEC monolayers. We find that mean HUVEC monolayer stiffness, as measured by atomic force microscopy, increases with increasing substrate stiffness:  $2.3 \pm 0.2$  kPa on 0.9 kPa gels,  $3.2 \pm 0.2$  kPa on 5.2 kPa gels, and  $4.4 \pm 0.3$  kPa on 100 kPa gels. However, when the monolayers are treated with TNF- $\alpha$  the effect of the substrate stiffness is abrogated and all monolayers show similar stiffness. Still, we have found that leukocyte migration on the HUVECs is biphasic with substrate stiffness, as our previous results on PA gels have shown.

**A-03 Joel Stavans, Weizmann Institute of Science*****Damped oscillations in the adaptive response of the iron homeostasis network of E. coli***

*Living organisms have often to adapt to sudden environmental changes and reach homeostasis. To achieve adaptation, cells deploy motifs such as feedback in their genetic networks, endowing the cellular response with desirable properties. We studied the iron homeostasis network of E. coli, which employs feedback loops to regulate iron usage and uptake, while maintaining intracellular iron at non-toxic levels. Using fluorescence reporters for iron-dependent promoters in bulk and microfluidics-based, single-cell experiments, we show that E. coli cells exhibit damped oscillations in gene expression, following sudden reductions in external iron levels. The oscillations, lasting for several generations, are independent of position along the cell cycle. Experiments with mutants in network components demonstrate the involvement of iron uptake in the oscillations. Our findings suggest that the response is driven by intracellular iron oscillations large enough to induce nearly-full network activation/deactivation. We propose a mathematical model based on a negative feedback loop closed by rapid iron uptake, and including iron usage and storage that captures the main features of the observed behavior. Taken together our results shed light on the control of iron metabolism in bacteria and suggest that the oscillations represent a compromise between the requirements of stability and speed of response.*

**Session B: Virus Assembly****B-01 Charles M. Knobler, University of California, Los Angeles*****What determines the size of a virus?***

*Viral genomes, are enclosed in a protein container, the capsid, which is usually icosahedral and which can be made up of many copies of a single protein. A number of viruses can self-assemble in vitro. When purified capsid protein and RNA are brought together in solution at an appropriate pH and ionic strength, they assemble spontaneously into structures that are identical to wild-type viruses. Moreover, capsid assembly can take place around anionic polymers or even nanoparticles, not just RNA, to form what are called virus-like particles (VLPs). This allows us to investigate experimentally the factors that control viral size, including the size, flexibility and charge of the packaged material and the charge and spontaneous curvature of the capsid protein.*

**B-02** **Sofía L. Alcaraz Estrada, Georgetown U Medical Center and CINVESTAV**  
**With Mark Irvin M. Manzano, Helios Cardenas, Selene Zarate, Rosa M. Del Angel,**  
**Robin Levis, R. Padmanabhan**

***Identification of temperature-sensitive mutants by using a dengue virus serotype 4 replicon system***

*The replicon systems of Flaviviridae family viruses have been used to study trans-complementation, adaptive mutagenesis, virus assembly and packaging, and to identify functional roles of the untranslated regions of the virus genome. The replicons contain all the genetic elements needed for RNA amplification, but they lack of the major part of the structural genes. Also they allow discrimination between two important processes in the virus life cycle, translation and replication. For dengue virus (DENV), there are four genetically related but serologically distinct serotypes and all of them cause the disease associated with DENV. To increase our understanding of the requirements needed for DENV replication the objective of this work was to generate a subgenomic Renilla luciferase (Luc) reporter base DENV serotype 4 Falgout strain replicon and test mutants for a temperature sensitive (ts) phenotype.*

*Seven mutants were generated by introducing single nucleic acids mutations in the NS3 (L1602F, S1632P), NS4b (A2482) and NS5 (N2583I, N2877H, K2924R, M3292I) genes. These replicons were electroporated into Vero cells, incubated at 35 °C, 37 °C and 39 °C and assayed for Luc activity as a function of time. None of the mutants presented a ts phenotype for translation. In the case of replication the mutants L1602F and S1632P presented a ts phenotype at 39 °C. The mutant N2583I showed a ts phenotype at 37 °C and 39 °C. The mutation N2583I is in the methyltransferase domain of NS5, near the binding site of SAM, the methyl donor for N-7 and 2'O methylation. Methyltransferase (Mtase) experiments were done with wild type and mutant recombinant protein and it was determined that the temperature sensitive phenotype of mutant 2583 is given by deficiency on N-7 activity. In view of the fact that the amino acid 2583 of the NS5 protein is not located at the functional sites of the Mtase domain, the influence of the mutation in long-range structural differences between WT and mutant proteins was analyzed by molecular dynamic simulations at 35 °C and 39 °C. The simulations analysis showed consistent differences between the WT and the mutant N2583I in the motion of the protein. Thus, our results suggest that the amino acid change in position 2583 may be not important for the structure of the protein but it may be disturbing the network motion of the molecule. Until now it is known that the N7 methylation reaction is achieved via substrate proximity, orientation and transition state stability, thus, changes in protein motion could be altering all these important parameters.*

**B-03** **Tomás López, IBT-UNAM**  
**With Daniela Silva, Norbert Perrimon, Susana López, Carlos Arias**

***The ubiquitin-proteasome system is necessary for efficient replication of rotavirus in cellular culture***

*Rotavirus is the major cause of severe gastroenteritis in young infants. To date there are two available vaccines, but pharmaceutical interventions are not in use. Rotaviruses are double-stranded RNA viruses with cytoplasmatic replication. Several of the aspects of the replicative cycle are not fully understand. To gain insights in the interactions between cell and rotavirus, and to identify new therapeutical targets, we developed a high throughput screen for rotavirus replication and proved the effect of siRNAs directed to more than 25,000 cellular genes over the viral replication. We identify 518 candidates; one of these candidates was the ubiquitin-*

proteasome system. To confirm this, we used pharmaceutical and molecular approaches to identify the events that require the ubiquitin-proteasome system. Activity of the proteasome is required to supply free amino acids and to perform efficiently the viral translation. A second event that is influenced by proteasome activity is the viral transcription. We found that MG132, a well-studied inhibitor of the proteasome, reduces the replication of the viral genome. These data suggest that protein degradation and/or ubiquitination of proteins are necessary for efficient RNA replication.

**B-04 Royá Zandi, University of California, Riverside*****Self-assembly of icosahedral, prolate and conical capsids***

*Virus particles come in many sizes and shapes and vary enormously in the number and nature of the molecules from which they are built. Amazingly enough, despite this tremendous diversity, most spherical capsids adopt the structures with icosahedral symmetry and the elongated capsids have almost always hexagonally ordered cylindrical bodies with hemispherical T-number caps centered along 5-, 3- and 2- fold axes. In this talk, I show that the remarkable well-defined geometry of spherical and prolate viruses is the consequence of free energy minimization of a generic interaction between the structural units of viral shells. I also discuss the conical structure of HIV capsids and show that the continuum theory of elastic shells combined with the non-equilibrium assembly process is able to predict the formation of structures pertinent to retroviruses (such as HIV). The minimal model of our assembly yields a unified one-dimensional phase diagram in which the appearance of spherical, irregular, conical and cylindrical structures of retroviruses is seen to be governed by the spontaneous curvature of protein subunits.*

**Session C: Materials****C-01 Abel Moreno, IQ-UNAM****Investigations into protein crystallization in the presence of a strong magnetic field**

*A new strategy is proposed for batch crystallization of proteins in solution-growth or gel-growth by using the batch method inside capillary tubes within magnetic fields. Four proteins with differing proportions of  $\alpha$ -helices and  $\beta$ -sheets, crystallized in five different crystallographic space groups, were studied, allowing an analysis of the anisotropy of the diamagnetic susceptibility of the peptide bond as well as the polarity of the space groups in a magnetic field of 11.75 T. The crystal quality is shown to be improved by using a strong magnetic field to orient protein molecules, and gel-growth (high concentrations of agar) to control the transport phenomena as well as crystal growth. Some advantages to increase the crystal quality for crystals from marginal conditions for X-ray diffraction, and disadvantages of the use of solution- and gel-growth (low concentration of agar) in magnetic fields, and their plausible applications to high resolution X-ray crystallography are discussed.*

**C-02 Mohammad F. Islam, Carnegie Mellon University*****Normal modes and density of states of disordered colloidal solids***

*The normal modes and the density of states (DOS) of any material provide a basis for understanding its thermal and mechanical transport properties. In perfect crystals, normal modes take the form of plane waves. In disordered systems, they can be complex and have never been*

determined directly in any experiment. I will show our recent measurement of the normal modes and the DOS in disordered colloidal solids: disordered colloidal crystals and colloidal glasses. The DOS shows Debye-like behavior at low energies and an excess of modes, or Boson peak, at higher energies. The normal modes take the form of plane waves hybridized with localized structures in the Debye regime. Interestingly, the disappearance of the longitudinal and transverse plane wave character of the modes near the Boson peak depends on the nature of disorder. Our approach shows how different types of disorder impact normal mode structure, DOS and elastic properties.

This work has been supported by NSF through DMR-0645596 and DMR-0619424, the Sloan Foundation and American Chemical Society Petroleum Research Fund.

**C-03 Luis F. Rojas-Ochoa, CINVESTAV****Assessment of direct interactions between casein micelles during milk acidification by diffuse light scattering**

Milk acidification causes the aggregation of casein micelles resulting in a gel-like state known as yoghurt. Here we present light scattering results of the optical properties of skim milk during yoghurt formation by addition of the acidifier glucono- $\delta$ -lactone (GDL). For this purpose, we implemented an experimental setup which allows for measuring in-situ the systems turbidity.

The experimental results were modeled by considering the propagation of light as a diffusive process, where information on the particle form and systems static structure is required. The form factor has been calculated with Mie theory for spherical particles, where micelles radius corresponds to the measured hydrodynamic radius. The static structure factor was calculated by solving the Ornstein-Zernike equation considering an effective potential between casein micelles which includes different contributions as Van der Waals attraction plus electrostatic and steric repulsions. The closure relation used is the soft-core mean spherical approximation (SMSA). We observe good agreement between experiments and our model, thus corroborating the assumption that aggregation of casein micelles during milk acidification is due primarily to the partial collapse of the brush layer over the micellar surface. Milk acidification reduces the electrostatic and steric repulsions thus allowing the Van der Waals attraction to overcome the repulsive forces. As the total potential becomes attractive, the distance between casein micelles is gradually reduced until they form a physical gel at a characteristic acidity of the system,  $\text{pH} \approx 4.8$ .

**C-04 Jesus C. Ruiz-Suárez, CINVESTAV  
With F. Pacheco-Vázquez****Granular matter: Lower density – more complexity**

When an object moves in a fluid, it experiences a drag force that depends on its velocity, its shape and the properties of the medium. From this simplest case to the motion of a flock of birds or a school of fish, the drag forces and the hydrodynamic interactions determine the full dynamics of the system. Similar drag forces appear when a single projectile impacts and moves through a granular medium, and there is a plethora of information in the literature about this phenomenon. However, the case in which a group of intruders impact a granular material has never been considered. Here we study the simultaneous impact and penetration of several intruders in a very low density granular medium. We find that the intruders move through the bed in a collective way following a cooperative dynamics, whose complexity resembles flocking phenomena in living systems or the movement of reptiles in sand, where changes in drag are

exploited to efficiently move or propel. Our results show that in the realm of extremely low densities, a granular medium yields like a fluid but retains the distinctive properties of its graininess.

**C-05 Steve Granick, University of Illinois**

**Clusters and helices from Janus particles**

*In areas from protein fibrosis to supracolloidal self-assembly, one finds ubiquitous helical structures. These can be imaged optically in the laboratory using “patchy” Janus particles – hydrophobic on one domain, hydrophilic elsewhere. The resulting self-assembled supracolloidal clusters and fibers have no counterpart for traditional particles whose energy depends solely on spacing. They offer a direction in which to look to design new reconfigurable materials, as well as on the chemistry side to explore reaction pathways at the single-particle level. This talk will also tentatively consider possible protein analogies.*

**Session D: Membranes – Experiment, Theory and Simulations**

**D-01 Gerard C. L. Wong, University of California, Los Angeles**

**Membrane topological transitions and human health: From antimicrobial peptides to apoptosis proteins**

*Pore forming peptides and proteins impinge a broad spectrum of phenomena in human health, ranging from innate immunity and cancer biology. In this talk, we will briefly describe several examples where physics-based approaches have been useful.*

*We examine the mechanism of mammalian defensins, a prototypical family of host defense peptides, and show how we can use soft matter physics to construct a general set of design rules for antimicrobials that punch holes in bacterial membranes but not in mammalian membranes.*

- 1. Apoptosis plays a key role in developmental biology and cancer biology. The Bcl2 family of proteins is responsible for the dominant intrinsic mitochondrial pathway for apoptosis. We will show how such proteins regulate apoptosis via membrane curvature mediated interactions.*

**D-02 Mathias Lösche, Carnegie Mellon University**

**High-resolution structures of intrinsically disordered systems: Protein-membrane interactions in health and disease**

*Biomembranes are amongst the most intricate, and most important, morphological structures in the cell. In their functional state, they are characterized by a high degree of intrinsic disorder. Sparsely-tethered lipid bilayer membranes (stBLMs) on solid supports mimic many relevant aspects of biological membranes. Molecular-scale studies of the interactions of peptides and proteins with such membrane models can provide clues to their function in health and disease. Neutron reflectometry (NR) offers unique possibilities to determine the high-resolution structure of intrinsically disordered membranes. Here, we discuss the association of the matrix domain of the HIV-1 Gag protein with stBLMs to study the complex membrane binding mechanism of the protein with the plasma membrane of host cells. This interaction constitutes a key event for the assembly of immature daughter particles in the viral replication cycle. The Gag matrix domain carries a myristoyl anchor, sequestered while the protein is dissolved in the cytoplasm, that is*

*believed to be released once the protein binds to PIP(4,5)P<sub>2</sub>, located on the plasma membrane. But how does the protein bind to the bilayer in the correct orientation for viral assembly? – With NR, we studied the orientation dependence and depth of insertion of the unmyristoylated Gag matrix domain at stBLMs and were thereby able to dissect the contributions to that interaction. With recently developed analytical tools we show that the binding orientation is highly specific and depends critically on the distribution of charges on the protein surface. This is verified by comparing the NR results with computations of the orientation dependence of the electrostatic interaction energy between the protein and the membrane.*

**D-03 Jemal Guven, ICN-UNAM*****Morphological defects in growing thin sheets***

*Defects will emerge in any slowly growing thin sheet whenever its modes of deformation are constrained to be unstretchable. A toy model is examined in which deformations are penalized by an energy quadratic in curvature. Unstretchability implies a constraint on the surface metric, enforced using a set of local Lagrange multipliers. These multipliers are identified with a conserved tangential stress that couples to the curvature of the sheet. Consider a circular sheet. If growth from the center is linear it will adopt a conical shape, its intrinsic geometry characterized by a surplus or deficit angle at its apex. Whereas this cone is circular in the case of a deficit, if this deficit is turned to surplus the disc folds into one of a infinite number of non-axisymmetric states labeled by an integer. These states are constructed explicitly, their energies as well as the distribution of stress within them determined. For each of these states, there is a critical value of the surplus angle beyond which the cone comes into self-contact. The stability of these states is examined and the ground state identified. Exponential growth will also be described briefly. In particular it will be shown that an initially axially symmetric shape -- a pseudosphere -- spontaneously develops undulations beyond some critical point in its growth.*

**D-04 Roland Faller, University of California, Davis*****What is the difference between a supported and a free lipid bilayer? Insights from Molecular Modeling***

*Supported Lipid Bilayers are an abundant research platform for understanding the behavior of cell membranes as they allow for additional mechanical stability and enable characterization techniques not reachable otherwise. However, in computer simulations these systems have been studied only rarely up to now. We present systematic studies on different length scales of the changes that a support inflicts on a phospholipid bilayer using molecular modeling. We characterize the density and pressure profiles as well as the density imbalance induced by the support. It turns out that the changes in pressure profile are strong enough that protein function should be impacted leading to a previously neglected mechanism of transmembrane protein malfunction in supported bilayers. We determine the diffusion coefficients and characterize the influence of corrugation of the support. We also measure the free energy of transfer of phospholipids between leaflets using the coarse-grained Martini model. It turns out that there is at equilibrium about a 2-3% higher density in the proximal leaflet. These results are in agreement with data obtained by very large scale modeling using a water free model where flip-flop can be observed directly. We are additionally characterizing the intermediate states which determine the barrier height and therefore the rate of translocation. We also study the influence of surface roughness and curvature on the behavior. Simulations in atomistic detail are performed for selected systems in order to confirm the findings.*

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**Session E: Molecular Interactions****E-01 Monica Olvera de la Cruz, Northwestern University*****The shape of ionic tethered membranes***

*The shape of elastic membranes and thin networks is of great importance in a variety of technological problems and biological processes. Homogeneous elastic shells with constraints can take a diversity of shapes via a buckling and/or crumpling mechanism. Electrostatics offers the possibility to generate membranes with new shapes and symmetries that are reversible. Elastic shells with positively and negatively charged components on their surface take various morphologies that can be readily controlled by changing ionic conditions including pH and/or salt concentrations. This electrostatic driven buckling mechanism provides a powerful tool for synthesizing nano-actuators or nano-switches. Experimentally and numerically obtained faceted ionic membranes will be shown and explained.*

**E-02 José Campos-Terán, UAM-Cuajimalpa****With Salvador Ramos, Jaime Mas-Oliva, Tommy Nylander, Rolando Castillo*****Surface force studies with apolipoprotein All alpha helices***

*To provide better understanding of how protein secondary structure affects protein-protein and protein-surface interactions, forces between amphiphilic  $\alpha$ -helical proteins (human apolipoprotein All) adsorbed on a hydrophilic surface (mica) were measured using an interferometric surface force apparatus (SFA). Forces between surfaces with adsorbed layers of this protein are mainly composed of electrostatic double layer forces at large surface distances and of steric repulsive forces at small distances. We suggest that the amphiphilicity of  $\alpha$ -helix structure facilitates the formation of protein multilayers next to the mica surfaces. We found that protein-surface interaction is stronger than protein-protein interaction, probably due to the high negative charge density of the mica surface and the high positive charge of the protein at our experimental conditions. Ellipsometry was used to follow the adsorption kinetics of this protein on hydrophilic silica and we observed that the adsorption rate is not only controlled by diffusion, but rather by the protein-surface interaction. Our results for dimeric apolipoprotein All are similar to those we have reported for the monomeric apolipoprotein Cl, which has a similar secondary structure but different peptide sequence and net charge. Therefore, the observed force curves seem to be a consequence of the particular features of the amphiphilic  $\alpha$ -helices.*



**E-03 Rolando Castillo, IF-UNAM**  
**With Erick Sarmiento-Gómez, Danaí Montalván-Sorrosa, David López-Díaz**

***Rheology and microrheology of fluids embedded with self-assembled thread-like structures: Wormlike micelles and fd virus***

The rheology and the microrheology of two fluid systems with threadlike-structures are studied and compared: (1) A micellar solution is made of a zwitterionic surfactant N-tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, sodium dodecyl sulfate, and salty water in the semidilute regime, and (2) Concentrated suspensions of fd virus. For microrheology experiments, we tracked the Brownian motion of particles set in the complex fluids using DWS. From the time evolution of the mean square displacement of particles, we could obtain the cage size where each particle is harmonically bound at short times, the long-time diffusion coefficient, and experimental values for the exponent that accounts for the broad spectrum of relaxation times at the plateau onset time found in the mean square displacement vs. time curves. From these curves,  $G'(\omega)$  and  $G''(\omega)$  were obtained for both fluids.

The micellar system, in a range of chemical composition, the solution behaves as a viscoelastic Maxwellian fluid at low frequencies. We present measurements of the elastic (storage) modulus and the viscous (loss) modulus varying the surfactant ratio ( $R = [SDS] / [TDPS]$ ), and how the Maxwellian relaxation time abruptly increases when the NaCl concentration is also varied. The effect of temperature in the viscoelastic solution is also studied. Shear stress vs. shear rate flow curves were measured under shear and stress control, for different micellar solutions with different composition, brine concentration, and temperature, showing a non-linear behavior. Flow curves present two stable branches corresponding to high and to low viscous fluids, separated by a stress plateau. Along the stress plateau, the micellar solution presents gradient shear banding. The DWS micro-rheological measurements allowed us to estimate the characteristic lengths of the WM network.

The fd virus suspensions present a viscoelastic behavior similar to that of polymers. We present measurements of the elastic (storage) modulus and the viscous (loss) modulus varying the virus concentration and ionic strength. The characteristic relaxation time increases as the virus concentration increases and decreases as the ionic strength increases.  $G''$  exhibits a power-law behavior at high frequencies, with the exponent changing from approximately 5/9 to 3/4, similar to what is observed in polymers, where the relaxation is first dominated by the Rouse-Zimm modes and then by the internal relaxation of individual Kuhn segments.

**Session F: RNA, Molecular Motors**

**F-01 Mauricio Carbajal-Tinoco, CINVESTAV**

***A model of RNA folding based on effective pair potentials***

We derive a set of knowledge-based potentials describing the interaction between pairs of nucleotides that belong to an RNA molecule. Such interaction potentials are then used as the main constituents of a simplified simulation model, which is tested in the description of small secondary structure motifs. Our simulated RNA molecules are consistent with the experimental structures obtained by NMR.

**F-02 Nicholas V. Hud, Georgia Institute of Technology*****A self-assembly approach to the proto-RNA world***

*Most current scientific theories for the origin of life contain the implicit assumption that RNA came before DNA and coded proteins (or some particular formulation of the “RNA world” hypothesis). However, just how the first RNA polymers would have assembled and replicated without the aid of protein enzymes remains an open question. We have hypothesized that the emergence of the first informational polymers of life is the direct result of molecular self-assembly on the early Earth. In particular, we have hypothesized that the first RNA-like polymers contained chemical building blocks that were similar in functionality to the contemporary building blocks of RNA, but distinct in that they were capable of forming low energy covalent bonds that facilitated polymer formation. We have also hypothesize that prebiotic molecules similar to molecules known today to intercalate contemporary nucleic acids, which we have termed ‘molecular midwives’, facilitated the assembly of RNA-like polymers by acting as nanometer-scale surfaces that templated base pair formation. This self-assembly approach to the origin of proto-RNA is showing promising results in the laboratory, and providing possible solutions to long-standing problems associated with the prebiotic synthesis of RNA, and could also provide a route to ‘bottom-up’ synthetic biology.*

**F-03 Maumita Mandal, Carnegie Mellon University*****DNA-mediated interactions of tethered vesicles***

*Riboswitches are structural elements that are present in the 5′-untranslated region of certain mRNAs of bacteria and eukaryotes. It is estimated that in *Bacillus subtilis*, 3% of the genes are controlled by riboswitches. These mRNA elements bind specific metabolites such as nucleobases, amino acids, vitamins and cofactors in the ligand binding domain to control gene expression of the adjacent gene. As the ligand binds to the phylogenetically conserved domain, it triggers an allosteric rearrangement in the expression platform that results in transcription termination, inhibiting ribosome binding or mRNA cleavage by ribozyme action. Although, several high resolution structures for the ligand binding domains have been reported, the dynamics of conformational switching in relation to their function as receptors for small molecules has only begun to be studied. Recently, we have used dual beam optical tweezers to study the force dependence and the kinetics of conformational switching in single molecules of a guanine-responsive riboswitch. The overall conformations of the riboswitch at physiological  $Mg^{2+}$  concentrations suggest that the leader mRNA exists in a mixture of conformations and is not pre-organized into a specific receptor structure. Our studies indicate that the ligand helps in nucleating the riboswitch core and thus stabilizes the structure. The real time folding-unfolding kinetics of a single molecule provide direct evidence to understand the cooperativity and the energetic coupling of  $Mg^{2+}$  and ligand-dependent structural conformations, that may be fundamental to other RNA-ligand dependent gene regulation.*

**F-04 Braulio Gutiérrez-Medina, IPICYT*****Measuring the torsional properties of molecular motors and biomaterials using optical tweezers***

*Optical tweezers have been an extremely powerful tool in the investigation of biological processes, particularly the activity of molecular motor proteins and processive enzymes, whose ba-*

*sis function involves converting chemical energy into motion or mechanical work. The ability to measure displacements with near Ångstrom resolution and to apply sub-picoNewton forces in a controlled manner makes optical trapping ideal to study the motion of biological molecules at the highest levels of precision. Force and displacement, however, are only half of the picture. There are a host of biological enzymes and motor proteins that generate torque and rotation as part of their primary activity. In addition, the fact that DNA is structured as a double helix implies that processing enzymes that move along a DNA template undergo rotation and generate torsional strain as a direct result of their function. In this talk, I will describe recent optical tweezers experiments that measure the torsional properties of the motor protein kinesin, performed by tracking the thermal angular motions of fluorescently-labeled beads bound to the C-terminus of the molecule. Testing kinesin motors immobilized on microtubules under varied nucleotide conditions allowed us to identify domains with varying degree of rotational flexibility, results that impose new constraints on kinesin walking models, and suggest a role for rotational freedom in cargo transport. I will also discuss the Optical Torque Wrench, an optical tweezers setup which has the ability to manipulate micron-sized objects, measuring force and displacement in a conventional manner, with the additional capacity of rotation, measuring torque and angular displacement with high precision (~1 pN nm of torque) at high bandwidth (~10-100 kHz).*

**Session G: Molecular Assemblies****G-01 Ting Xu, University of California, Berkeley*****Directed assemblies of peptide-polymer conjugates toward functional biomolecular materials***

*Peptides and proteins are nature's building blocks and offer a great library of chemical and structural diversity. Upon conjugating to polymers, forming peptide-polymer conjugates, synergistic co-assembly of natural and synthetic building blocks may lead to hierarchical assemblages with features down to the molecular level and contain inherent biological, electronic and optical properties and may lead to functional biomolecular materials for catalyst, filters, lithography, biocompatible implants and regenerative medicines. I will discuss two recent developments in directed assemblies of peptide-polymer conjugates in solution and in thin films. Specifically, I will present some recent efforts in fabricating sub-nm porous membranes and nearly monodisperse virus-like nanoparticles.*

**G-02 Miguel Costas, FQ-UNAM  
With Rolando Castillo, Ángel Piñeiro*****Cyclodextrin-based self-assembled floating nanotubes***

*Native  $\alpha$ -cyclodextrin ( $\alpha$ -CD) is found to spontaneously form films at aqueous solution/air interfaces. Shape-response measurements to volume perturbations on drop hanging from a capillary indicate that temperature and sodium dodecyl sulfate (SDS) concentration strongly modify the viscoelastic properties of such films. By using isothermal titration calorimetry (ITC), Brewster angle microscopy (BAM), atomic force microscopy (AFM), dynamic surface tension (DST), viscoelastic modulus (VM) and molecular dynamics (MD), it is shown that the film consist of self-assembled nanotubes whose building block are cyclodextrin dimers ( $\alpha$ -CD<sub>2</sub>) and  $\alpha$ -CD<sub>2</sub>-SDS<sub>1</sub> complexes.*

**G-03 Joel Ireta Moreno, UAM-Iztapalapa*****Microsolvation of polypeptide helices***

*Helix formation is one of the crucial steps in the folding process of proteins. Folding a solvated peptide from its extended to a helical conformation implies a partial desolvation of the peptide bond. In this talk, we present an estimate of the energetic cost for desolvating the peptide bond and the effect of desolvation on the formation of an alpha and a  $3_{10}$  helix. Such estimates are based on density functional theory electronic structure calculations of microsolvated infinitely long polyalanine chains in helical and polyproline II conformations. Explicit water molecules are used for microsolvating the peptide. According to our findings it will be argued that desolvation of the peptide bond favors helix formation in water. However changing the bulk water dielectric constant favors polyproline II conformation. The implication of these results on deciphering which forces are driving the protein folding process will be discussed.*

**G-04 Markus Deserno, Carnegie Mellon University*****Studying folding of helical peptides in the microcanonical ensemble***

*Through a microcanonical study of different helical peptides we analyze the thermodynamics of secondary and tertiary structure formation and their impact on folding cooperativity. For short alpha-helices, the transition is driven by secondary structure formation alone; tertiary interactions are irrelevant and the transition is of two-state type. In contrast, the folding of longer helices may require the decondensation of hydrophobic residues from a non-native collapsed core before the native state is reached; in this case, the interplay between secondary and tertiary structure formation determines the nature of the transition.*

**Session H: Membrane Thermodynamics****H-01 Sarah Veatch, Cornell University****With Benjamin Machta, Ethan Chiang, David Holowka, Barbara Baird*****Lipid rafts reach a critical point***

*Multicomponent lipid bilayer membranes can contain two coexisting liquid phases, named liquid-ordered and liquid-disordered. Recently, we demonstrated that large (micron-scale) and dynamic critical fluctuations are found in 'simple' ternary bilayer membranes prepared with critical compositions. Remarkably, robust critical behavior is also found in compositionally complex vesicles isolated directly from living cell plasma membranes. This finding strongly suggests that cells tightly regulate plasma membrane protein and lipid content to reside near a critical point and that critical fluctuations provide a physical basis of functional membrane heterogeneity in living cells at physiological temperatures. We are currently probing for critical fluctuations in intact RBL mast cells using high resolution imaging techniques (scanning electron microscopy and super-resolution fluorescence localization microscopy). In addition, we are investigating possible structural and functional consequences of plasma membrane criticality using computational approaches, and are testing these predictions experimentally using the model system of IgE mediated signaling in RBL mast cells.*

**G-02 Said Eduardo Aranda Espinoza, Universidad Autónoma de Zacatecas**

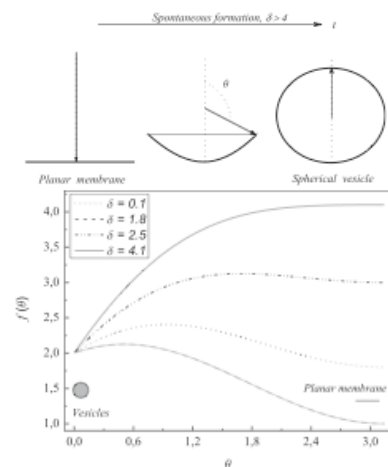
**Morphological transitions of vesicles induced by AC electric fields**

The effects of electric fields on cells have been abundantly demonstrated and used for cell manipulation. These effects include cell fusion, rotation, alignment, dielectrophoretic manipulation, pore formation in the membrane, levitation, re-orientation of the cell, and cell deformation. This complex behavior of cells in electric fields is exploited in many application fields such as drug delivery, gene transfer and hybridization of cells for vaccine development. In order to study the effects of electric fields on cells we need to understand how electric fields affect the plasma membrane. Here we use giant unilamellar vesicles to mimic the cell membrane. When subjected to alternating electric (AC) fields in the frequency range  $10^2 - 10^8$  Hz, giant lipid vesicles attain oblate, prolate and spherical shapes and undergo morphological transitions between these shapes as one varies the field frequency and/or the conductivities  $\sigma_{in}$  and  $\sigma_{ex}$  of the aqueous solutions within and outside of the vesicles. Four different transitions are observed with characteristic frequencies that depend primarily on the conductivity ratio  $\sigma_{in}/\sigma_{ex}$ . Known theoretical models are not able to describe all of these morphological transitions.

**G-03 Ivan Santamaría-Holek, UNAM**  
With L. Martínez-Balbuena, E. Hernández-Zapata

**Thermo-kinetic model for vesicle formation and pore dynamics**

We propose a free energy expression accounting for the formation of spherical, ellipsoidal and sphero-cylindrical vesicles from planar lipid membranes and derive a Fokker-Planck equation for the probability distribution describing the dynamics of vesicle formation. We find that formation may occur as an activated process for small membranes and as a transport process for sufficiently large membranes. We give explicit expressions for the Arrhenius and non-Arrhenius transition rates, and the characteristic time of vesicle formation in terms of the relevant physical parameters. We also study the dynamics of pores formed in these vesicles and show that our model is more general than previous ones.



**G-04 Marjorie L. Longo, University of California, Davis**

**Xerogel, lipopolymer, and ethanol control lipid phase behavior**

We demonstrate that the characteristic of substrates (e.g. high curvature) or a polymer can strongly influence the phase behavior of a mixed lipid layer offering some advantages and disadvantages that can be mitigated. First, we show that high curvature ( $r \sim 50$  nm) in a silica xerogel layer can be used to induce lipid demixing or intrabilayer transport over large areas. Second, we develop an approach to counteract substrate-induced tension in mica-supported lipid bilayers. Consequently, we use AFM imaging to construct a lipid/sterol/ethanol phase diagram consistent with unsupported bilayers. Third, we observe complicated phase behavior in lipid/lipopolymer binary monolayers including stoichiometric complex formation with possible implications to bilayer phase behavior.

**Posters****P-01 Guillermo Ivan Guerrero-Garcia, Northwestern University  
With E. Gonzalez-Tovar, Monica Olvera de la Cruz*****Effects of the ionic-size asymmetry around a charged nanoparticle: Unequal charge neutralization and electrostatic screening***

*In this work we study the consistent inclusion of ionic size-asymmetry for a wide range of macroparticle charges in the primitive model of an electrical double-layer around a spherical colloid using (1) Monte-Carlo simulations, (2) hybrid integral-equation formalism of hypernetted-chain (HNC) and mean-spherical approximation (MSA), and (3) Gouy-Chapman theory modified for unequal ionic-radii [1]. In our simulations for a weakly charged macroion, we observe surface charge amplification from adsorption of like-charged ions, as well as charge reversal due to overcompensation of the bare nanoparticle charge by counterions. When the nanoparticle charge increases, we detect both asymmetric neutralization and asymmetric electrostatic-screening that depend on the sign of the macroion's valence. Specifically, there exists a higher reduction of the original bare charge and a smaller electrostatic potential for the case of negative nanoparticles with positive small counterions, versus the case of positive nanoparticles with negative large counterions. These coarse-grained results are in agreement with the predictions of asymmetric charge renormalization [2], in which the aqueous solvent is explicitly taken into account. Results from the Gouy-Chapman theory modified for unequal ionic radii differ notably from our obtained Monte-Carlo data, while good agreement exists between simulation results and HNC/MSA-treatment findings.*

[1] G. I. Guerrero-Garcia, E. Gonzalez-Tovar and M. Olvera de la Cruz, *Soft Matter* (2010).

[2] P. Gonzalez-Mozuelos and M. Olvera de la Cruz, *Phys. Rev. E* **79**, 031901 (2009).

*Supported by the NSF (DMR-0520513, MRSEC program at Northwestern University), and by CONACYT, Mexico, through grant CB-2006-01/58470 and PROMEP, Mexico.*

**P-02 César Aguirre, FQ-UNAM  
With L. Olguin, Miguel Costas*****Enzyme kinetics of trypsin using isothermal titration calorimetry***

*UV or fluorescence are commonly used to study enzyme kinetics. Often, to use these techniques substrates need to be modified by addition of a chemical group or moiety which can be spectroscopically followed. These modifications might interfere with the enzymatic reactions and limit our knowledge to only a few substrates. Isothermal Titration Calorimetry (ITC) is a thermodynamic technique that directly measures the heat released or absorbed during a chemical process. Typically, ITC is employed to study protein-ligand interactions. However, it can also be used to measure the heat evolved during a enzyme catalyzed reaction, which is proportional to the rate of reaction. The heat associated (enthalpy) to the advance of the reaction is calculated directly integrating the area under the signal. ITC is then a useful tool to study enzyme reactions that cannot be followed by spectroscopic techniques. To corroborate the validity of ITC technique, the hydrolysis of N-Benzyl-Arginine-Ethyl-Ester catalyzed by trypsin was followed by UV spectroscopy and ITC, finding that the rate constants determined by both methods are statistically identical. We have studied the trypsin kinetics with another two substrates, namely ethyl- and methyl esters of L-arginine (LAEs), which cannot be determined by spectroscopy.*

**P-03 Benjamin B. Machta, Cornell U**  
**With Stefanos Papanikolaou, James P. Sethna, Sarah L. Veatch**

***Implications of criticality in cell membranes***

Here we present a minimal model of plasma membrane heterogeneity that combines criticality with connectivity to cortical cytoskeleton. Our model is motivated by recent observations of micron-sized critical fluctuations in the 2d Ising Universality class in plasma membrane vesicles that are isolated from cortical cytoskeleton [1]. We incorporate criticality using a conserved order parameter Ising model coupled to a simple actin cytoskeleton interacting through point-like pinning sites. In our model small ( $r \sim 20$  nm) and dynamic fluctuations at physiological temperatures arise from criticality. Including connectivity to cortical actin disrupts large fluctuations and macroscopic phase separation at low temperatures ( $T \leq 23^\circ\text{C}$ ) and provides a template for long lived fluctuations at physiological temperature ( $T = 37^\circ\text{C}$ ). In addition, we use analytical techniques from conformal field theory and numerical simulations to investigate the form of effective forces mediated by the membrane's proximity to criticality. We show that the range of this force is maximized near a critical point and we quantify its usefulness in mediating communication using techniques from information theory. More generally, we demonstrate that critical fluctuations provide a physical mechanism to organize and spatially segregate membrane components by providing channels for interaction over large distances.

1. Veatch, S.L., et al., *ACS Chem Biol* **3**, 287 (2008).

**P-04 Catalina E. Haro-Pérez, UASLP**

***Dynamic arrest in charged vesicle suspensions exhibiting large-scale structural heterogeneities***

Suspensions of charged liposomes are found to exhibit typical features of strongly repulsive fluid systems at short length scales, while exhibiting structural heterogeneities at larger length scales that are characteristic of attractive systems. We model the static structure factor of these systems using effective pair interaction potentials composed of a long-range attraction and a shorter range repulsion. Our modeling of the static structure yields conditions for dynamically arrested states at larger volume fractions, which we find to agree with the experimentally observed dynamics.

**P-05 Prabhanshu Shekhar, Carnegie Mellon**  
**With Frank Heinrich, Mathias Lösche**

***Optimization of tethered bilayer lipid membranes of mixed lipid compositions***

Biological membranes are of overarching importance for all aspects of cell structure and function in living organisms. Planar tethered bilayer lipid membranes (tBLMs) are synthetic membrane models stabilized by the proximity of a solid substrate—typically a Si wafer or a glass slide — that enhances its resilience and long-time stability by orders of magnitude.<sup>1,2</sup> To combine these practical advantages with the suitability as a membrane model, they incorporate a nanometer-thin hydration layer between the bilayer and the substrate ensuring its fluidity with in-plane dynamics similar to that in vesicles.<sup>3</sup>

These tBLMs are required for a variety of studies of protein-membrane interactions, for example, the assembly of HIV virus in infected cells promoted by the GAG protein, cell entry of bacterial toxins that illicit diphtheria and tetanus, and the damaging effects of the Alzheimer's pep-

tion, amyloid, on lipid membranes.<sup>4</sup> Sometimes, these proteins interact with anionic lipids in membranes that consist primarily of zwitterionic lipids and/or cholesterol. The biophysical properties of these tBLMs vary significantly with bilayer composition and require a well-described model system.

In this work, we establish tBLMs composed of binary and ternary lipid mixtures as more complex, and hence more realistic, membrane models. We also studied the effect of different tether molecules on our model systems. We report a structural and compositional characterization by neutron reflectometry and electrochemical impedance spectroscopy of the asymmetric tBLMs that comprise various lipid compositions including cholesterol. A new composition-space model was developed to interpret neutron reflectivity data of such systems, enabling us to get an elaborate description of our system. Such a detailed structural and compositional assessment is a prerequisite for a better understanding of the studies of protein-membrane interactions.

[1] D. J. McGillivray, et al., *Biointerphases* **2**, 21 (2007).

[2] F. Heinrich, et al., *Langmuir* **25**, 4219 (2009).

[3] S. Shenoy, et al., *Soft Matter* **6**, 1263 (2010).

[4] G. Valincius, et al., *Biophys. J.* **95**, 4845 (2008).

**P-06 Pablo Agustín Vázquez Montejó, UNAM  
With Jemal Guven**

***Semi-flexible polymers confined to membranes***

We develop a theoretical framework to describe the conformation of a semi-flexible polymer confined within or onto a surface. The relevance of this problem resides in the ubiquity of confinement in biological systems, for instance in cellular compartments or in viral capsids. It is also present in the conformation of biopolymers such as DNA whose transcription and replication is governed by specific binding of proteins. In our model the energy associated to the polymers is quadratic in its curvature (Euler elastica) and the confinement constraint is implemented using a local Lagrange multiplier in the variational principle. We derive the corresponding Euler-Lagrange equations describing the constrained system. As an application of this framework, the conformation of a closed semi-flexible polymer of length  $2\pi R$  within a sphere of radius  $1 < R$  is described.

**P-07 Michael J. Skaug, UC Davis  
With Roland Faller, Marjorie L. Longo**

***Correlating obstructed diffusion with obstacle morphology using single-molecule tracking in supported lipid bilayers***

Biophysical research has shown that membrane phospholipids and proteins diffuse not only under normal Brownian diffusion, but with confined and anomalous behavior. We are motivated to understand this anomalous diffusion because it may be involved in many cell functions. We have used single molecule tracking on phase separated, supported lipid bilayers to investigate the origin of this unusual diffusion. DSPC forms gel phase domains that act as obstacles to diffusion in the DOPC continuous liquid phase. Tracking single fluorescent molecules in the fluid phase provides dynamic information beyond just an ensemble diffusion coefficient and by controlling the gel domain morphology we can correlate the observed single molecule diffusion with the obstacle characteristics. We show that the anomalous diffusion exponent and the dynamic coefficient decrease as the obstacle area density increases. This is justified in terms of



*the obstacle correlation length and the experimental time scale. We tested our results by producing Monte Carlo simulated trajectories using experimentally measured obstacle fields and we found good agreement. The correlation we find between obstacle morphology and diffusion behavior will aid studies that cannot directly characterize the obstacles to diffusion.*

**P-08 Hilda J. Mercado-Urbe, CINVESTAV  
With A. Angulo-Sherman**

***The existence of an isosbestic point in dielectric spectra of water***

*Although the water has been studied extensively since the last past century, it continues to be a subject of great interest because it has special properties and a relevant role in biological functions. One of the most used techniques to study water is the dielectric spectroscopy. Normally, the works with this method are carried out at frequencies higher than 1 MHz. Here, we have analyzed the behavior of water in the range from 20 Hz to 1 MHz. We designed an experimental device based on a cylindrical capacitor that allows us to measure dielectric properties of water as a function of temperature. We found that there is a frequency where the value of the dielectric constant is independent of temperature. We call this the isosbestic point. Since a biological cell is a capacitive system, we consider that the existence of this point could be important to understand the robustness of cellular function.*

**P-09 Kimberly M. Stroka, U Maryland  
With Helim Aranda-Espinoza**

***Endothelial cell stiffness depends on the presence of neighbors***

*Cell mechanics have been shown to depend on many exogenous factors, including substrate ligands and substrate stiffness. When cells form aggregates, they are also affected by the presence of their neighbors; for example, in a monolayer cells are smaller and there are cell-cell adhesions in addition to cell-substrate adhesions. How cell-cell contacts affect the mechanical properties of cells has received very little attention. Here, we use atomic force microscopy (AFM) to measure the mechanical properties of live human umbilical vein endothelial cells (HUVECs) with varying degrees of cell-cell contact, including monolayers, networks, and single cells. We find that spreading area and cellular stiffness depend on degree of cell-cell contact. Specifically, single cells are stiffer and larger in area than cells in a monolayer, while cells within a network are stiffer and larger than both monolayers and single cells. Further, using AFM and bright-field images, we simultaneously measure cell stiffness and area during spreading, and find that HUVECs stiffen as they spread. We show that these results together indicate that the presence of neighbors influences cellular stiffness. To corroborate these results, we disrupt cell-cell junctions in two ways, using a VE-cadherin antibody and cytochalasin B, and find that in both cases the stiffness of cells in a monolayer increases to approach that of single cells. These results further indicate the importance of cell-cell adhesions in governing cell mechanics in a monolayer. We also investigate the organization of F-actin and focal adhesions, and our results suggest that a balance between cell-cell adhesion and cell-substrate adhesion exists and contributes to maintenance of tension within the cells. Our results signify the importance of cell-cell adhesions in signaling to the mechanical machinery of the cell, a process which may vary in conditions when cell-cell contact changes, such as during wound healing, angiogenesis, or immune cell transmigration.*

**P-10 Jos W. Zwanikken, Northwestern U  
With Rastko Sknepnek, Monica Olvera de la Cruz*****Ion induced attractions between responsive nanoparticles***

*The interactions between nanometer-sized particles in an ionic solution are often described as a complex sum of pair-wise contributions. Not only the bare Coulomb and Van der Waals interactions, but also the presence of other constituents is paramount for the phase behavior. We study the effective attractions between spherical nanoparticles in a correlated electrolyte solution, induced by the surrounding ions that weakly bind to the particle surface. In contrast to polymers that generate depletion forces because of entropic effects, we find that ions can induce attractive forces by fluctuations of the surface charge, and more pronounced, by an effect that is reminiscent of a capillary wetting. In molecular dynamics simulations of the primitive model we observe the formation of ionic bridges between nanoparticles that are well understood within the framework of density functional theory. We argue that these short-ranged forces can easily overcome like-charge repulsions between identical nanoparticles. Our results can be meaningful for the stability of protein solutions and salt-specific interactions between proteins.*

**P-11 Cuitláhuac Chávez-Peña, IB-UNAM  
With Octavio Tonatíuh Ramírez, Laura A. Palomares*****Adeno-associated virus-like particle analysis using size exclusion chromatography coupled with dynamic light scattering detection***

*Adeno-associated virus (AAV) is one of the most promising candidates as vector for gene therapy. The characteristics of the AAV capsid make it a suitable starting material for nanobiotechnology applications. The AAV capsid has icosahedral symmetry and is composed of 60 monomers of three proteins (VP1 to VP3) with diameters between 18 and 25 nm. The use of adeno-associated virus for either medical or nanotechnological applications requires a complete characterization of capsid preparations, as well as the development of purification and analysis methodologies that ensure product quality, safety and consistency. For this, here we propose the use of dynamic light scattering (DLS) coupled with size exclusion chromatography (SEC). Recombinant AAV capsids (VLP) were produced in the insect cell-baculovirus expression system utilizing a recombinant baculovirus (BacCap) containing the VP gene. VLP were purified by either CsCl gradient centrifugation or by ion exchange chromatography. The resulting samples were analyzed by gel permeation HPLC in a Bio Suite 250 UHR column and a DLS detector. Fractions eluted from the column were collected and tested by dot blot with an antibody specific for assembled AAV capsids. Particles of different sizes were detected and their size was determined by DLS without the need of column calibration. Both purification schemes used resulted in a peak with an elution time of 8.5 min and particles with a size of 20.1 nm. Finally, AAV VLP preparations were characterized by batch measurements of DLS under different physicochemical conditions. Coupling of SEC with DLS is capable of resolving and detecting the presence of AAV VLP in different samples in a very efficient way so the combination of both techniques can be used for either analytical or purification purposes with online monitoring of the particle size distribution. This technique is a powerful tool to study self-assembled materials.*

**P-12 Agnieszka Kalinowski, Carnegie Mellon  
With Siddharth Shenoy, M. Lösche, Kris N. Dahl*****Intermolecular and intramolecular interactions and their role in Lamin A accumulation at the nuclear membrane in human aging and premature aging disease***

*Hutchinson-Gilford progeria syndrome (HGPS) is a premature aging syndrome causing systemic defects. It shows close analogies with normal aging at the molecular and cellular level. It was reported that  $\Delta 50$  lamin A, the mutant form of an intermediate filament protein in the nucleus, causes lamin accumulation at the nuclear membrane resulting in mechanical anomalies.<sup>1</sup> It is unknown if this membrane accumulation is primarily caused by the deletion of a 50 AA exon or the retention of a post-translational farnesylation on the mutant. We use purified protein fragments, the lamin A tail domain that lacks interactions with other lamins in the structural protein network that supports the nuclear membrane, to quantify changes in protein stability and protein-membrane interactions in the cell and with synthetic membrane models. Circular dichroism indicates no gross structural difference between the wt and  $\Delta 50$  lamin A tail domains, but the unfolding temperature is increased in the latter. This suggests topological differences between the  $\Delta 50$  lamin A and the wt protein which may be responsible for the more stable laminar filament formation in vivo. In addition, the effect of the retained farnesyl group on the protein's membrane interaction will be discussed.*

*Supported by the Progeria Foundation and an NIH-NRSA fellowship (1 F30 AG030905).*

*[1] Dahl, K.N., et al., Proc. Natl. Acad. Sci. USA 103, 10271 (2006).*

**P-13 Danaí Montalván-Sorrosa, IF-UNAM  
With Erick Sarmiento-Gomez, Jaime Mas, Rolando Castillo*****Rheology and microrheology of rodlike fd virus suspensions***

*High concentration water suspensions of rodlike fd virus were prepared using standard techniques of molecular biology. Low frequency rheology using mechanical rheometry, and high frequency microrheology using diffusing wave spectroscopy, were measured for virus suspensions at different fd concentrations and salt concentration. The fluid presents a viscoelastic behavior where the loss modulus is higher than the storage modulus at low frequencies, and after a crossover the storage modulus is larger. At high frequencies, we observed a transition similar to that found in polymers from the Rouse-Zimm relaxation modes to the internal bending relaxation modes of single Kuhn segments.*

**P-14 Ajaykumar Gopal, UC Los Angeles  
With Defne E. Egecioglu, Marc Niebuhr, A. L. N. Rao, Charles M. Knobler, William M. Gelbart*****Viral RNA molecules are unusually compact***

*We present the results of several complementary experimental techniques and coarse-grain molecular dynamic simulations that allow for comparisons of the sizes and shapes of long single-stranded (ss) RNA molecules with different sequences, compositions, and lengths. The lengths are in the range of several thousands of nucleotides, and the compositions are those of ssRNA viral genomes and of sequences chosen at random from a yeast genome. The experimental techniques include measurements of: electrophoretic mobilities in native gels; hydrodynamic radii by fluorescence correlation spectroscopy (FCS); radii of gyration and distance dis-*

tributions by small-angle X-ray scattering (SAXS); and real-space configurations by cryoelectron microscopy (cryo-EM). From these results we are able to show that viral sequences lead to three-dimensional (3D) sizes that are distinctly smaller than those of non-viral sequences with the same nucleotide length and composition. By changing buffer conditions we demonstrate further that the size differences correlate with relative compactness of the associated secondary structures. Finally, we show that viral RNA molecules, under *in vitro* assembly conditions, are slightly larger than the capsids in which they become spontaneously packaged. These results are confirmed by 3D coarse-grained structures simulated by molecular dynamics and predicted directly from the primary nucleotide sequence.

**P-15 Cem Yolcu, Carnegie Mellon  
With Ira Z. Rothstein, Markus Deserno**

### ***Effective theory for Casimir interactions on a membrane***

Particles bound to fluid surfaces can interact with each other by modifying the fluctuation spectrum of the surface in a way that depends on the relative positions of these particles. This effect is the classical analog of the Casimir forces, well known from quantum electrodynamics. While in many cases the bare surface Hamiltonian is simple, in the sense that it is quadratic in the degrees of freedom such that the partition functional integral can be evaluated directly, the presence of the bound particles breaks translational symmetry and renders the problem technically much more difficult. Here we argue that the local effect of the adhering finite-sized particles can be systematically mimicked by point particles whose interaction with the surface is described by generalized polarizabilities. Using this trick, the problem can be rewritten as a much simpler effective field theory that can be treated by standard perturbation methods. We thereby recover many existing results in the literature in a much more efficient way. Moreover, we demonstrate that the simplicity of the method permits the treatment of more complicated situations, such as three-body corrections, in a straightforward manner.

**P-16 Mauricio Comas-Garcia, UC Los Angeles  
With Ruben D. Cadena-Nava, Charles M. Knobler, William M. Gelbart**

### ***Measuring the packing efficiency of single-stranded viruses***

All viruses are made up of a single-molecule-thick protein shell known as capsid that encloses the genome of the virus; in most instances the capsid is either icosahedral or cylindrical. The viral genome is either DNA or RNA, which can be single or double stranded; most genomes are single-stranded RNA (ssRNA). ssRNA viruses can also be classified by the number of molecules that make up the genome, and are referred to as monopartite (one molecule) or multipartite (many). The capsid proteins of many ssRNA viruses have positively charged N-termini that project into the capsid interior where they can interact with the negatively charged RNA. This electrostatic interaction is known to provide a driving force for spontaneous virus assembly, but 3D size and shape of the RNA is also expected to play a role. These facts raise important questions like: Why do some viruses split their genome into several molecules? Why do some viruses package their multipartite genome into one capsid while others package the individual RNA molecules into separate capsids? What controls the size of a viral capsid? In this work we ask, in particular: How does the packaging efficiency of ssRNA viruses change as a function of genome length? In order to explore this problem we investigate the *in vitro* self-assembly of nucleocapsid from purified RNA and capsid protein. We prepare a mixture of full-length and trun-

*cated ssRNA molecules and measure how much of the shorter molecule is packaged relative to the full-length genome when both are in solution and competing for capsid protein.*

**P-17 J. Roger Vega-Acosta, IF-UASLP****With Ruben D. Cadena-Nava, L. A. Pinedo-Torres, Jaime Ruiz-Garcia, Laurence Lavelle, M. Phillips, M. Gingery, William M. Gelbart, Charles M. Knobler*****Structure and stability of the self-assembly products of the capsid proteins of the cowpea chlorotic mottle virus (CCMV)***

*We describe the self-assembly of capsid proteins of the CCMV virus under different pH and ionic strength conditions. The self-assembly is carried out in the absence of the viral genome. In good agreement with previous measurements, a wide range of polymorphs can be identified by electron microscopy, among them single and multiwalled shells and tubes. The images are analyzed with respect to size and shape of aggregates and evidence is given that equilibrium has been achieved, allowing a phase diagram to be constructed. Some structures that have not been previously reported are also described. The range and stability of the self-assembly products can be understood in terms of electrostatic interactions yielding insight in the way they affect the spontaneous curvature of protein networks and the relative stabilities of pentamers and hexamers.*

**P-18 Ruben D. Cadena-Nava, UC Los Angeles****With Rees Garmann, Charles M. Knobler, William M. Gelbart*****Self-assembly of hybrid virus particles***

*One of the many remarkable things about viruses is that some of them can be made in vitro from purified components. In the simplest cases, there are only two components – the capsid protein and the RNA genome. Furthermore, spontaneous self-assembly of a nucleocapsid – a virus-like particle – also occurs when the RNA genome is replaced by non-genomic RNA or even by synthetic anionic polymer.*

*We report the in vitro self-assembly of hybrid virus particles formed by the capsid protein of cowpea chlorotic mottle virus (CCMV) and single-stranded RNAs (ssRNAs) with lengths ranging from about 3000 nucleotides (nt) – the wild-type CCMV RNA length – to 9000 nt. The goal is to explore the effect on capsid size of the length of the ssRNA packaged, and to establish a procedure for determining the best conditions for achieving 100% RNA packaging. In this study genomic RNAs of brome mosaic virus (BMV) with a length of 3234 nt, of tobacco mosaic virus (TMV) (6395 nt), and of a Sindbis-derived RNA replicon containing an enhanced yellow fluorescent protein (EYFP) gene (9000 nt) were each shown to self-assemble efficiently into virus-like particles when combined with CCMV capsid protein in a ratio of 1:6 (wt:wt). These results provide a basis for developing new protein expression systems and vector strategies for delivery of genes and vaccines.*

**P-19 Miguel A. Valdez, Universidad de Sonora  
With Ana B. López-Oyama, Jaime Ruiz-García*****Interaction of the cationic peptide bactenecin with phospholipids at the air-water interface***

*In this work we investigate the adsorption of the antimicrobial cationic peptide bactenecin on monolayers of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) at the air-water interface as a function of NaCl concentrations in the subphase. We show that the effect of the salt concentration on DPPC monolayers is a monotonic decrease of the liquid condensed-liquid expanded (LC-LE) coexistence region. By contrast, the effect of the bactenecin adsorption at the DPPC monolayer not only removed the LC-LE coexistence region plateau, but also shifted the DPPC isotherms to higher pressures and increased the compressibility of the DPPC/bactenecin monolayers with respect the pure DPPC monolayer. The effect of mixed DPPC with 1,2-dimyristoyl-sn-glycero-3-phospho-(1'-rac-glycerol) sodium salt (DMPG) was also investigated. An increase of surface pressure was achieved as a consequence of electrostatic interactions with the negatively charged DMPG. Analysis of the domain structure, obtained by Brewster angle and atomic force microscopy, indicates that the salt concentration in the subphase build an electrostatic barrier, increasing the rigidity of DPPC monolayers and limiting the bactenecin adsorption at the LC-LE phase coexistence. The peptide adsorption was also investigated by Raman spectroscopy.*

**P-20 Laura M. Fernández-Díaz, IF-UNAM  
With S. Ramos, Rolando Castillo*****Langmuir monolayers of thiolated copper nanoparticles***

*Molecular interactions allow the self-assembly of nanoparticles at the air/water interface forming Langmuir monolayers that present a variety of phases. Even though gold and silver nanoparticles Langmuir monolayers have been widely studied, less research has been done to date to describe monolayer of nanoparticles made with other metals, namely copper. This investigation is aimed to the synthesis of thiol functionalized copper nanoparticles and the study of their Langmuir monolayers. A simple method for the copper clusters synthesis in solution was used. Infra red spectroscopy confirms the chemisorption of alkanethiol on copper surface via -SH group. The nearly spherical morphology (3-5 nm) and the narrow size distribution of the nanoparticles are determined by transmission electron microscopy. Langmuir monolayers of copper nanoparticles were developed and observed by using Brewster angle microscopy. Preliminary results show the presence of three different phases. Gas phase at low area densities, further compression shows a phase transition to a liquid like phase, and in some cases apparently there is a next transition at high lateral pressures, just before the collapse.*

**P-21 Edgar Rogelio Alvizo-Paez, IF-UASLP**

**With Jose Manuel Romo-Herrera, Humberto Terrones, Mauricio Terrones, Jaime Ruiz-Garcia**

***Foam-like 2D networks of nitrogen-doped multi-walled carbon nanotubes formed through self-assembly***

*This work present a physicochemical study in two dimensions of nitrogen-doped multiwall carbon nanotubes (CNx) via the Langmuir-Blodgett technique (LB). LB allows us to vary the CNx surface density at the air/water interface and measure how their isotherms change as a function of time, as the CNx diffuse from the bulk to the interface. Self organization at the air/water interface was observed in-situ by Brewster Angle Microscopy (BAM). In addition, CNx films were transferred onto modified silicon and mica substrates and analyzed via atomic force microscopy (AFM) and scanning electron microscopy (SEM), with to determine their nanoscopic arrangement. The average thickness of transferred films was measured by ellipsometry as well, together with the optical reflectance in the UV-vis region and Raman spectra. We show that the two-dimensional foam-like CNx networks can be transferred onto the solid substrates, which may have potential applications in conducting and transparent nanoelectronic circuits, hydrogen storage devices, field emission components, and emission photo diodes.*