that present both amine and carboxylic groups on the surface. To test the reactivity of these groups they were conjugated with fluorophores and biomolecules by EDC-NHS chemistry. The resulting structures were analyzed by electrophoresis, scanning electron microscopy and surface enhanced Raman scattering measurements. The impact of these results and the resulting nanoparticle versatility will be discussed.

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Branched, Amphipathic Peptides that Self Assemble into Nanovesicles

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Lipid based vesicles have traditionally been used as a formulation strategy to deliver drugs but non-lipid based polymer vesicles that show better stability, specificity and tunability are gaining more importance lately. Peptide vesicles are one such example. We have designed and synthesized a set of relatively short (15, 19 and 23 residue), branched, amphipathic peptides that self-assemble into nano-vesicles. When pairs of such lyophilized peptides with different lengths are co-dissolved in deionized distilled water they undergo supramolecular assembly to form nano-vesicles (50 - 200 nm in diameter, as determined by transmission electron microscopy). A 500 μL solution of the peptide mixture with an individual peptide concentration of 1.6mM yielded in excess of 1×10^{10} vesicles. Analytical ultra centrifugation data suggests a reproducible peptide association with a weighted average S value of 8. According to circular dichroism data, the assembled peptides adopt predominantly a beta-sheet conformation. The peptides can be dissolved under conditions that promote a monomeric helical conformation. In an alternate solvent system they switch to a beta-sheet conformation. The ability to initially dissolve the sequences as monomers allows for controlled mixtures with desired ratios. These peptide vesicles are capable of entrapping various solutes. We have delivered 5,6 carboxyfluorescein into Human lens epithelial cells grown on cover slips. We are currently exploring the ability to control the size of the vesicles formed by altering the ratios of the different chain lengths in a given peptide mixture. These are potential drug delivery vehicles for targeted delivery and we envision packaging genetic material into these peptide vesicles.

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Evaluation of Selected Kissing-Loops as Building Blocks in RNA Nano Design

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We are developing computer-aided methods for designing nano-scale structures built of RNA. As the first step we created the RNAJunction database, which is a repository of RNA junctions (i.e. internal loops and kissing-loop interactions), and which can be used as a source of building blocks for nanostructures. These building blocks, combined with idealized fragments of A-form helices, can be used by two programs developed in our laboratory, NanoTiler and RNA2D3D, to produce desired 3D nano structures. In the initial stages of nano-scale shape design, the building blocks are treated as rigid or near-rigid objects. However, since experimental data shows that RNA accommodates its shape to the constraints of larger structural contexts, we are adding analysis of the flexibility of our building blocks to the overall design process. Here we present examples of RNA-based nanostructure designs, with the stress on the characterization of the structural flexibility of the building blocks and potential approaches to controlling these characteristics. Examples focus on the use of kissing loops (KL) in nanostructure design, since they show potential for introducing angular junctions necessary to produce regular polygonal shapes. We compare and contrast reprogrammed KLs based on the HIV-1 KL complex, already experimentally proven, with the dynamic behavior of other kissing loops some of which have been used in experimental assembly and others which are being experimentally evaluated. In some cases flexible KLs appear to be absolutely required for the assembly of larger shapes, while in others an alternative design, bypassing geometrically useful but potentially unstable KLs can be a better strategy.

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Characterization of RNA Nano Design Structures by Steered Molecular Dynamics Simulations Approach

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RNA nano particles are built by self-assembly of various RNA building blocks. Modified RNAs containing carbocyclic sugars constrained to north/south sugar conformations rigidify nucleotides due to their locked sugars. Modified RNA building blocks can be used for RNA nano particle design to increase stability and alter the helical properties. Steered molecular dynamics (SMD) simulations were used to characterize an unmodified and modified RNA dodecamer and an HIV kissing loop complex. As the unmodified RNA dodecamer was elongated by an applied external force along the axial direction, an overstretching transition was observed whereby a double stranded force-extension curve showed a transition to that of a single strand. The backbone delta angles in the unmodified RNA dodecamer started to increase when elongated by more than 60%. The modified dodecamer, however required more force beyond 60% elongation due to the resistance induced by the constrained sugars. This is due to the increased resistance to change of the backbone delta angles associated with the modified bases. In the unmodified HIV kissing loop complex, the kissing loop base pairing started to break down when the elongation reached 70% and the applied force started to drop when the elongation reached 120% due to kissing loop separation. The change in conformation and the backbone delta angles in the pulled stem of the unmodified complex is larger than its counterpart stem. However, the backbone delta angles of the modified HIV kissing loop complex showed smaller changes in both stems due to the constrained sugars. These results indicate the plausibility of characterizing RNA nano-design building block components by the application of external forces and in particular suggest the possibility of using modified bases in RNA structure to control the stability of RNA-based nano designs.

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Nanopatterning at the Service of Single Molecule Assays

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Today, the manipulation and integration of objects with nanometric dimensions is essential for a great number of applications. In biology and medicine, the study of structural dynamics in individual molecules or other key cellular processes is often limited by the low throughput of current methods. Here, we will demonstrate how nanopatterning could yield improvements relative to current practice for single molecule assays, by increasing the density and organization as opposed to random deposition. In fact, we have explored the combination of soft-lithography with a directed capillary assembly technique [1]. As a proof of concept, we have demonstrated that by using this methodology we are able to control the assembly of different objects ranging from cells, to molecules and nanoparticles, at accurate positions and at high yield while preserving their functionality [2-4]. As an extension of these results, we will show that we are capable of multiplexing sequences in a field of view and capable of including imaging-enhancing structures colocated with DNA tethers. This will lead to the construction of a robust experimental platform allowing massively parallel data collection at the single molecular level in real time and under various conditions.

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Possible Origin of Life between Mica Sheets

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Many problems with the origin of life are solved by the hypothesis that life emerged between mica sheets. Ancient natural "books" of mica sheets provided secure nano-environments, endless energy sources, confinement chemistry effects, huge entropy reductions, and grids of anionic mineral sites bridged by exchangeable potassium ions (K^+).

The following scenario is proposed:

Simple mechanical Work provided energy for covalent bond formation by mechanochemistry. Solar energy cycles and water movements powered up-and-down movements of mica sheets. A carbon-carbon bond's energy at room temperature is comparable to 6 nanoNewtons of force, moving 1 Angstrom in distance (Figure).

Mica's up-and-down movements pressed on protocells, blebbing off 'daughter'protocells. Blebbing-off has been observed in wall-less L-form bacteria