between cells. Metropolis Monte Carlo (MMC) simulations based on DAH predicted the emergence of long-lived structures (cell sheets, toroidal and tubular constructs) in accord with experiments. The MMC method, however, does not describe time evolution. We propose a kinetic Monte Carlo (KMC) approach, where transition rates are associated with possible rearrangements of cells. The system is represented on a lattice, with sites occupied either by cells or by volume elements of cell culture medium. We associate rates to swapping cells with nearest neighbors of different types (cells or medium). The new approach was tested against experiments on cell sorting within an aggregate composed of two cell types. In quantitative studies, we determined the time evolution of the interfacial area between two fusing spherical cell aggregates experimentally, analytically and by KMC simulations. In the analytic approach, we used continuum hydrodynamics to describe the coalescence of two identical, highly viscous liquid droplets, and obtained good agreement with experiments on smooth muscle cell aggregates. Apart from the early stages of fusion, the KMC method predicted a fusion pattern similar to the experimental one. Comparison with measurements allowed relating KMC transition rates to experimental time scales. Our results indicate that the KMC method can give an accurate account of the time evolution of complex cellular structures, thus it may be a useful tool for tissue engineering applications. Work supported by NSF-056854.

3269-Pos Board B316

Fully Biological Bioprinted Blood Vessel Substitutes

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Cardiovascular disease is a leading cause of death and often requires vascular reconstruction. There is considerable clinical need for alternatives to the autologous vein and artery tissues used for vascular reconstructive surgeries, lower limb bypass, arteriovenous shunts and repair of congenital defects to the pulmonary outflow tract. Engineering new tissues, ideally from the patient's own body cells to prevent rejection by the immune system, is a rapidly growing field that rests on three pillars: cells, supporting structures (or scaffold) and stimulating biological environment. However the use of scaffolds has often been associated with chronic inflammation and impaired tissue-remodeling and maturation. In this respect understanding the physical principles of biological self-assembly is essential for developing efficient strategies to build living tissues and organs. Here we exploit well-established developmental processes (such as tissue fusion, spreading or sorting phenomena) to engineer small-diameter blood vessels. We introduce a novel automated rapid prototyping method (bioprinting) that allows the building of three-dimensional custom-shaped tissue and organ modules without the use of any scaffold, thus making the final construct fully biological, as well as structurally and functionally closer to native tissues. Conveniently prepared bio-ink units (multicellular spheroids or cylinders composed of single or several cell types) are delivered into the bio-paper (a hydrogel support material) to build linear and branching tubular structures of small diameter (down to 0.9 mm OD). Structure formation takes place by the post-printing fusion of the discrete units. Upon removal of the support material, the fused construct is matured in perfusion bioreactor under pulsatile flow until desirable biomechanical (burst pressure, compliance) and biochemical (e.g. ECM) properties develop. Such constructs could fulfill the crucial need for small diameter vascular grafts and provide new strategies for vascularization of tissues for transplantation.

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Amphiphilic Peptides That Self Assemble into Nanomicelles and Vesicles

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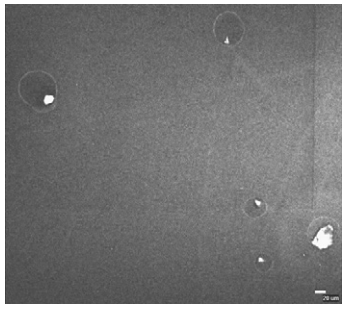
Self-Assembling peptide nanovesicles are attractive candidates for drug delivery. Here we report the characterization of specific amphiphilic peptides (up to 23-amino acids in length) that undergo supramolecular assembly to form both mono- and hetero-assemblies that form nanomicelles and larger vesicles (150nm) in aqueous solutions. Depending on the peptide's composition and the pH of the aqueous medium during assembly, the peptides adopt either a micellar or vesicular structure. Simple amphipathic sequences adopt a micellar structure (<50nm) at low to neutral pH. When pairs of lyophilized peptides with different lengths are co-dissolved in an unbuffered Carboxyfluorescein solution at a 1:1 molar ratio, they self-assemble into small vesicles that are visualized using a confocal microscope. These intact vesicles average about 150nm in size (as determined by confocal images) and are capable of entrapping solutes. CD and FTIR analyses of such mixtures indicated a tendency of the peptide to adopt a beta sheet secondary structure. Isothermal Titration Calorimetry (ITC) revealed the Critical Aggregation Concentration (CAC) for the individual peptides to be less than 1mM, which is a useful property during drug delivery. These nanostructures can be used as models for further developments.



3271-Pos Board B318

High Throughput Lipid Bilayer Technologies

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Measurements of ion channels are important for scientific, sensing and pharmaceutical applications. Reconstitution of ion channels into lipid vesicles and planar lipid bilayers for measurement at the single molecule level is a laborious and slow process incompatible with the high throughput methods and equipment used for sensing and drug discovery. A recently published method of lipid bilayer formation mechanically combines lipid monolayers self-assembled at the interfaces of aqueous and apolar phases. We have expanded on this method by vertically orienting these phases and using gravity as the driving force to combine the monolayers. As this method only requires fluid dispensation, it is trivially integrated with high throughput automated liquid-handling robotics. In a proof-of-concept demonstration, we created over 2200 lipid bilayers in three hours. We show single molecule measurements of technologically and physiologically relevant ion channels incorporated into lipid bilayers formed with this method.

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Construction of a Bioprinted Fully Biological Nerve Graft

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Annually over 200,000 peripheral nerve surgeries are performed in the U.S. alone. Many of these procedures require grafts to bridge the severed nerve. Autologous nerve is the gold standard for providing a temporary support across which axons regenerate. Although successful at 80%, the autograft procedure has several drawbacks including the limited number of available nerves, the loss of function and /or sensation at the donor site and the need of multiple surgeries. Synthetic or natural nerve guidance hollow tubes have been used successfully as scaffolds for small gaps (<3cm) but regeneration fails over longer distances. As a result, tissue engineering has emerged as a promising alternative. Based on recent studies, synthetic and autologous tubes failure has been linked to low density of supporting cells such as Schwann cells and the lack of longitudinally-oriented structural features, which favor Bunger's bands-like formation and axonal growth by mimicking endoneural architecture. In addition, axonal growth can be impaired by inflammatory and immunological responses triggered by the implanted scaffold.

We present here a novel tissue engineering technology that is based on principles of developmental biology and employs bioprinting, This automated rapid prototyping method allows for creating well-defined architectural features, without any scaffold, thus making the final construct completely biological as well as structurally and functionally closer to native tissues. Spherical or cylindrical bio-ink units (composed of Schwann and bone marrow stem cells) are delivered according to a computer scrypt together with agarose rods, as support material units. Structure formation takes place by the post-printing fusion of the discrete units. The geometrical parameters of those tubes, such as wall thickness, diameter, and number of lumens can easily be controlled. Such constructs could fulfill the crucial need for larger nerve grafts.

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Influenza A Nucleoprotein Detection by a Novel Immuno-Interferometric Sensor

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Rapid detection and identification is imperative to combat known or emerging infectious agents. This novel immuno-interferometric sensor utilizes the specificity and selectivity of antibody-antigen interactions to detect and identify a specific influenza viral component in a label-free manner. Primary antibodies to the nucleoprotein of Influenza A (IFA) were oriented utilizing a previously reported polymer- protein interaction system of poly(methyl methacrylate) (PMMA, CAS# 9011-14-7) and biolinker protein G′. This unique noncovalent adsorption method resulted in increased primary antibody orientation, and