2008-Pos Board B27
Investigating the Interactions between Aβ and Amylin: Insight into the Link between Alzheimer's and Type II Diabetes
Yifat Miller, Michal Baram.
Ben-Gurion University, Beer-Sheva, Israel.
The self-assembly of peptides is associated with protein aggregation in numerous incurable diseases, including amyloid β (Aβ) in Alzheimer's disease (AD), α-synuclein in Parkinson's disease (PD), and amylin in type II diabetes (T2D). Experimental evidence led to the hypothesis that cross-amyloid interactions, e.g., interactions between Aβ and amylin also play a critical role in protein aggregation. Structure-based characterization of the interactions between two types of amyloids is fundamental to understanding the self-assembly mechanism that exists between them and may pave the way to elucidate the link between two diseases, e.g. T2D and AD. Combining computational tools with experimental data this lecture illustrates for the first time the interactions between Aβ and amylin oligomers. Identifying the specific ''hot regions'' bindings of amylin with Aβ demonstrates polymorphic Amylin-Aβ complexes. This study may provide insight into the link between diseases and may pave the way to the development of drugs that could ameliorate neurodegenerative diseases by interrupting the interaction between the relevant proteins and hence reducing protein aggregation. The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2011) under grant agreement 303741.

2009-Pos Board B28
Interactions of Urea and Trehalose with an Amyloidogenic Peptide Sequence from ß-Lactoglobulin
Nicolas Taulier[1,2], Stéphane Abel[3], Marcel Waks[2,4], Wladimir Urbach[5,6].
[1]CNRS, Paris, France, [2]UPMC Paris, Paris, France, [3]CEA, Saclay, France, [4]INSERM, Paris, France, [5]ENS, Paris, France, [6]Université Paris Descartes, Paris, France.
A number of human neuropathies are linked to protein aggregation leading eventually to the deposition in tissues of insoluble aggregates referred as amyloid structures. Such insoluble deposits result from monomeric units assembled by a complex multistep process into oligomers and in fibrils with cross-secondary structures. Non-pathogenic naturally occurring amyloids aggregate as a generic property of their peptide backbone given the right experimental conditions. A number of them termed functional amyloids regulate physiological functions in various domains. The spontaneous oligomerization in water and in presence of urea of the ß-lactoglobulin heptapeptides H_(146) IRLSFN_(152) (6 and 12 peptides) has been previously investigated by atomistic molecular dynamics (MD) simulations in explicit water using GROMACS and the GROMOS53A6 force field. Here we examine further in detail the interaction of two widely used cosolvents: urea, a common denaturant and trehalose, a polyol stabilizing proteins by extensive hydrogen networks and preventing the formation of aggregates. Understanding the role of the osmolytes should provide insights into the general mechanism for ordered to aggregation-dependent transition. The results obtained illustrate the delicate balance between interpeptide, peptide-solvent, and solvent-solvent interactions. The studied osmolytes increase the conformational stability of the peptides by increasing the number of peptide-osmolyte hydrogen bonds at the expense of peptide-water ones. The conformational stability of the 12 peptide aggregate is similar in the three solvents due to the number of intrapeptide hydrogen bonds within its hydrophobic core. Isothermal compressibility results comfort the above mechanism. In addition the existence of possible water channels within the aggregates has been examined in water and in the presence of cosolvents. The extent and role of solvation/desolvation at interfaces during the assembly process is assessed.

2010-Pos Board B29
Lifetime of Major Histocompatability Complex Class I Membrane Clusters is Controlled by the Actin Cytoskeleton
Yael Lavi[1], Michael Edidin[2], Levi A. Gheber[3].
[1]Ben Gurion University, Raanana, Israel, [2]Johns Hopkins University, Baltimore, MD, USA, [3]Ben Gurion University, Beer Sheva, Israel.
Lateral heterogeneity of cell membranes has been demonstrated in numerous studies showing anomalous diffusion of membrane proteins; it has been explained by models and experiments suggesting dynamic barriers to free diffusion, that temporarily confine membrane proteins into microscopic patches. This picture, however, comes short of explaining a steady state patchy distribution of proteins, in face of the transient opening of the barriers. In our previous work we directly imaged persistent clusters of MHC-I, a type I transmembrane protein, and proposed a model of a dynamic equilibrium between proteins newly delivered to the cell surface by vesicle traffic, temporary confinement by dynamic barriers to lateral diffusion, and dispersion of the clusters by diffusion over the dynamic barriers. Our model predicted that the clusters are dynamic, appearing when an exocytic vesicle fuses with the plasma membrane and dispersing with a typical lifetime that depends on lateral diffusion and the dynamics of barriers. In a subsequent work we showed this to be the case. Here we test another prediction of the model, and show that changing the stability of actin barriers to lateral diffusion changes cluster lifetimes. We also develop a model for the distribution of cluster lifetimes, consistent with the function of barriers to lateral diffusion in maintaining MHC-I clusters.
Acknowledgment:
Support of this research by Grant #2009345 from the US-Israel Binational Science Foundation to M.E. and L.A.G. is gratefully acknowledged.

2011-Pos Board B30
Protein-Based Hierarchical Suprastructures Derived from κ-casein Amyloid Fibrils and their use for Neuronal Differentiation
Jiyeong Chun, Ghibom Bhak, Ji-Hye Lee, Kookheon Char, **Seung R. Paik**.
Seoul National University, Seoul, Korea, Republic of.
Functions are diversified by producing hierarchical structures from a single raw material. Protein-based suprastructures are considered to be versatile nanoscale materials particularly useful at the biological interface as their chemical natures could be easily modified. Their intrinsic biocompatibility allows them to be the junctional materials possibly employed between living cells and inanimate objects. In this respect, biologically compatible milk protein of κ-casein has been employed to fabricate higher-order suprastructures. In the presence of dithiothreitol and heat treatment, κ-casein transforms into amyloid fibrils with distinctive morphology attributable to mechanism-based fibrillar polymorphism. As the fibrils elongate to yield high aspect ratio during high-temperature incubation, the resulting fibrils laterally associate into liquid crystalline state by forming two-dimensional fibrillar array. Following a desalting process, the fibrillar arrays turn into three-dimensional matrix of hydrogel which could be selectively disintegrated by subsequent salt treatment. The hydrogel was demonstrated to be a matrix capable of exhibiting controlled release of bioactive substances like retinoic acid, which led to temporal and spatial control over the differentiation of neuronal cells. Therefore, the hierarchical suprastructure formation derived from the single protein of κ-casein producing one-dimensional protein nanofibrils, two-dimensional liquid crystalline state, and three-dimensional hydrogel could be widely appreciated in various areas of nanobiotechnology including drug delivery and tissue engineering.

Protein Assemblies & Aggregates III

2012-Pos Board B31
Sticky-Sphere Mixture Model for Light Scattering from Concentrated Eye Lens Protein Mixtures
George M. Thurston, Michael M. Bell, David S. Ross, Maurino P. Bautista, Carrie N. Lahnovych.
Rochester Institute of Technology, Rochester, NY, USA.
We use a sticky-sphere mixture liquid structure model to analyze static light scattering efficiency data obtained from aqueous mixtures of gamma and alpha crystallin eye lens proteins. The model incorporates (i) hard-sphere interactions between alpha crystallins, leading to short-range ordering and transparency at high concentration, (ii) short-range attractive interactions between gamma crystallins, which can produce intense light scattering and liquid-liquid phase separation, and (iii) both excluded-volume interactions and short-range attractions between alpha and gamma crystallins, which also sensitively affect transparency [Dorsaz:2009,Dorsaz:2011]. We derive general expressions for the scattered light intensity within the model, and compare the model with data from aqueous gamma/alpha mixtures. We show that the sticky-sphere mixture model can provide accurate representations of the observed static light scattering cross sections, including their concave-down dependence on alpha/gammaB composition at intermediate concentrations, combined with the concave up and more complicated, temperature-sensitive dependence on relative protein composition at high, more physiological protein concentrations [Thurston:2006]. We use the model to help study possible implications for molecular mechanisms of cataract, by changing gamma-gamma, gamma-alpha, and alpha-alpha interactions. The sticky-sphere mixture model exhibits non-monotonic dependence of light scattering intensity and thermodynamic stability on gamma-alpha attraction strength, consistent with simulation and perturbation theory [Dorsaz:2011]. The model predicts that gamma-alpha mixture light scattering is quite sensitive to gamma-alpha interactions, consistent with previous analysis of a congenital cataract [Banerjee:2011]. The sticky-sphere mixture model is useful for quantitatively analyzing light scattering of concentrated aqueous crystallin mixtures, relevant for understanding lens cytoplasm.