2008-Pos Board B27
Investigating the Interactions between Aβ and Amylin: Insight into the Link between Alzheimer’s and Type II Diabetes
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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 β-Lactoglobulin
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 in and 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 β-lactoglobulin heptapeptides H₁₄(146) IRSLF₁₅(152) (6 and 12 peptides) has been previously investigated by atomicistic 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.

2008-Pos Board B26
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.

2011-Pos Board B30
Protein-Based Hierarchical Suprastructures Derived from κ-casein Amyloid Fibrils and their use for Neuronal Differentiation
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 nature could be easily modified. Their intrinsic biocompatibility allows them to be the functional 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 formation of two-dimensional liquid crystalline phases. Following a desolvation 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-dimensionally 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
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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 [Doraz:2009,Doraz: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 [Doraz: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 [Bane-rjec:2011]. The sticky-sphere mixture model is useful for quantitatively analyzing light scattering of concentrated aqueous crystallin mixtures, relevant for understanding lens opacification.