gained increased flexibility. In summary, the weak thermal stability of cold-adapted enzymes can be enhanced by substitutions such as $W^{208}Y$, which confer the stability on the catalytic site at ambient temperatures.

3381-Pos Board B109
Thermodynamic Stability of an Aging Proteome
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How much oxidative damage can a proteome withstand before a critical threshold is reached? What defines this threshold? The accumulation of oxidized protein is a universal feature of an aging organism, however a quantitative understanding of the effects of physiological levels of oxidation on proteome stability is lacking.
Taking advantage of a growing body of data on length, charge, and stability distributions of entire proteomes, we develop a first-principles thermodynamic model of the effects of oxidation on the stability of proteins within an aging cell. By determining the equilibrium fraction of unfolded protein as a function of both oxidative stress and temperature, we predict that a small subset of proteins is largely responsible for straining an organism's protein homeostasis machinery. Furthermore, by looking at functional enrichment within this subset, we identify the protein classes that are expected to be the most sensitive to oxidation-induced destabilization.

3382-Pos Board B110
Investigation of Smart Responses of Human Serum Albumin in Fever Condition: An In Vitro Approach
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Human body core temperature is regulated at about 37°C by physiological adaptations. Increase of body temperature to 42°C has great effects on all systematic functions. These alterations ultimately can lead to fatal consequences.
Biological responses of human body proteins to fever condition is astonishing, especially those with significant role in body homeostasis regulation such as human serum albumin. In this research, structural and functional changes of human serum albumin by temperature increment up to 42 °C are studied via fluorescence spectroscopy, circular dichroism (CD), UV spectroscopy, and pH metery methods. In addition, Coamoxyclave, Acetaminophen and Fluoxetine were used as potential probes for determining these fine structural and functional changes.
The findings refer to less carrier activity and structural alterations of albumin accompanied by homeostatic mechanism activations such as salt and solutes exertion (osmotic) adjustments. Importance of this characteristic aspect of albumin can be considered in treatment of fever by chemical drugs. In conclusion, albumin plays crucial role as a smart molecule in stabilizing body temperature by its fine conformational modifications.

3383-Pos Board B111
Characterization of FGF-1 Mutant, K126D
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Fibroblast Growth Factor-1 is a 16 kiloDalton heparin-binding protein whose function involves signaling cells for responses such as cell growth, differentiation, endurance, and response to trauma. FGF-1 also has restorative effects like wound healing, angiogenesis, and nerve repair. Wild type FGF-1 has a short half-life in vivo, and denatures at physiological temperature. Due to its instability and potential for therapeutics, a more stable form of FGF-1 is desirable.
The purpose of the research study is to characterize the FGF-1 mutant, K126D using a series of techniques like CD, Fluorescence Spectroscopy, Differential Scanning Calorimetry, thermal denaturation, NMR spectroscopy, trypsin digestion, and ANS titration. These techniques will be used to assess the degree of stability of K126D as compared to wild type FGF-1. In addition, cell proliferation assays will be performed to determine how the mutation affects the activity of FGF-1.

3384-Pos Board B112
Biophysical Characterization of Therapeutic Proteins for Early Prediction of Manufacturability
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Biopharmaceuticals or therapeutically relevant proteins have become one of the fastest growing parts of the pharmaceutical industry. These innovative molecules are much more complex than conventional drugs and their processing is much more demanding. Assessing, at a very early stage in the development process, the ease of manufacture (the manufacturability) would allow the candidates proteins to be ranked and thus help controlling the cost-effectiveness of new drugs. Our research project aims to identify critical properties of protein candidates allowing the prediction of their behaviour in large-scale bioprocesses. Our multidisciplinary approach combines computational analysis (Molecular Dynamics simulations), the pilot-scale production and the biophysical characterization of a set of Fragment antibody (Fab) mutants.
This allowed the identification of regions of unstable structure helping to predict the stability of Fab candidates prior to experiments. Extensive aggregation kinetics were measured at a wide range of temperature, pH and ionic strength allowing the determination of a model for Fab aggregation and the development of a rapid micro-scale Fragment antibody aggregation screening method.

3385-Pos Board B113
The Heat Released by a Chemical Reaction Locally Enhanced the Enzyme Diffusion
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It has been one hundred years since Michaelis and Menten characterized the substrate concentration dependence of an enzyme-catalyzed reaction. In the intervening years, detailed catalytic mechanisms have been established for many different enzyme families, and it has been well established that enzymes increase reaction rates by lowering the activation energy of chemical processes. Although some enzymes are known to form transient covalent structures with their substrates, it is generally accepted that they are unaffected by the reaction process. Recently, it has been shown that the diffusivity of enzymes increases in a substrate-dependent manner during catalysis. Although this observation has been reported and characterized for several different systems, the precise origin of this phenomenon is unknown.
In this presentation we quantitatively demonstrate the mechanistic link between enhanced diffusion and the heat released in the reaction using single molecule fluorescence correlation spectroscopy data analyzed within the framework of a stochastic theory. We show that the magnitude of the diffusion change is proportional to the enthalpy of the reaction. This study offers a novel perspective on the effect of chemical reactions on their catalysts and suggests future experiments to explore how the local heat released at each turnover affect an enzyme's internal degrees of freedom.

3386-Pos Board B114
Lipid Disequilibrium Destabilized a Subset of Membrane Proteins
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Hundreds of distinct lipids, of varying concentrations, assemble to form biological membranes. The most abundant, phospholipids, varies according to head group structures, acyl chain length and double bounds. In eukaryotes, lipid compositions can differ widely among organelles. In most cases, the biological significance of these differences remains unclear. However, links between disease states and lipid disequilibrium have been proposed. It was reported by several groups that change in the ratio of the most two abundant phospholipids, phosphatidylcholine/phosphatidylethanolamine (PC/PE), might cause non-alcoholic fatty liver disease (NAFLD). Recently, we reported on how budding yeast cells respond to and cope with PC/PE disequilibrium. Using lipidomic, genomic, and proteomic technologies, the data revealed that the adaptive cells responded by remodeling the protein homeostasis network without restoring lipid composition. We termed this process the membrane stress response (MSR). Interestingly, we observed that some transmembrane proteins (TP) were strongly up- and down-regulated at the genomic and proteomic levels, respectively. Diverse candidate proteins were analyzed from normal and mutant cells to characterize their stability. Results suggest the stability of certain mature TP is affected from lipid imbalance. Furthermore, premature degradation of the candidates directly affects ER functions such as protein translocation and degradation if not for the intervention of the MSR.