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Title: The Achilles' Heel of "Ultrastable" Hyperthermophile Proteins: Submillimolar Concentrations of

SDS Stimulate Rapid Conformational Change, Aggregation, and Amyloid Formation in Proteins

Carrying Overall Positive Charge

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Abstract: Low concentrations (<3.0 mM) of the anionic surfactant sodium dodecyl sulfate (SDS) have been

shown to induce the formation of amyloid fibers in more than 20 different mesophile-derived proteins in the cationic state. It is not known whether SDS has similar effects on hyperthermophile-derived proteins, which are otherwise thought to be "ultrastable" and inordinately resistant to structural perturbations at room temperature. Here, we show that low (<4.5 mM) concentrations of SDS rapidly induce the formation of aggregates and amyloid fibers in five different ultrastable Pyrococcus furiosus proteins in the cationic state. We also show that amyloid formation is accompanied by the development of a characteristic, negative circular dichroism band at $\sim\!\!230$ nm. These effects are not seen if the proteins have a net negative charge or when higher

concentrations of SDS are used (which induce helix formation instead). Our results appear to reveal a potential weakness or "Achilles' heel" in ultrastable proteins from hyperthermophiles. They also provide very strong support for the view that SDS initially interacts with proteins through electrostatic interactions, and not hydrophobic interactions, eliciting similar effects entirely regardless of protein molecular weight, or structural features such as quaternary structure or

tertiary structural stability.

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