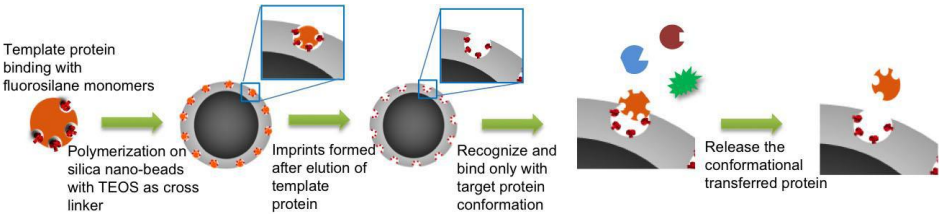
Detection of misfolded proteins through molecular imprinting

Molecular imprinting is a method of forming an artificial recognition element for a target molecule by using that target molecule as a template. A target molecule, such as a biomarker for disease, is added to a resin (polymer) that is cured, followed by removal of this target, leaving complimentary imprint sites. A handprint in cement tends to best fit the original hand; likewise, on the molecular scale, the original target molecules tend to fit best into their own imprint sites. Dr. David Britt of Utah State University and his collaborators have applied this technology to discriminate between conformational isomers of a target protein—that is, the same protein, but in two different shapes. This would be analogous to a handprint with the fingers open versus the same hand imprinted as a fist. Misfolded proteins are responsible for a range of neurological diseases, including scrapie, mad cow, and CFJ, in sheep, cattle, and humans, respectively. The disease state arises as misfolded proteins tend to self-assemble into insoluble plaques.

This USDA-NRI funded project allowed assembling an international team, consisting of researchers from Cranfield University, U.K., The University of Utah, and Utah State University. The researchers developed a molecular imprinting process in which a native protein could be distinguished from a geometrically distinct version of the same protein. This work represents a significant step toward developing rapid analytical methods to detect misfolded proteins, such as the prion protein causing mad cow disease.



It has been demonstrated that the fluorosilane chemistry induces conformational changes in proteins, favoring a conformation where the protein adopts "helical structure". Proteins, such as prion that cause neurological disease, exhibit a high degree of "sheet-like" structure. Thus, it may be possible to use imprinted fluorosilane polymer films as catalysts that favor reformation of alpha-helical structure in misfolded proteins. The Figure here depicts the process that constructs protein imprint sites on nano-beads that bind a misfolded protein and, through interactions with an imprint pocket, induce the protein to readopt the correct conformation.

Turner, N., X. Liu, S. Piletsky, V. Hlady, D.W. Britt, *Recognition of conformational changes in b-lactoglobulin by molecularly imprinted thin films,* Biomacromolecules, 8(9); 2781-2787, **2007**.

Invention Disclosures: 1 patent pending

Contributing Agencies: USDA/CSREES