Electrostatically triggered hydrophobic self-assembly of protein hydrogels

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Hydrogels are extensively used in medical applications due to their fundamental biocompatibility and intrinsic similarities to the extracellular matrix of certain tissues[1,2]. Biological hydrogels have been synthesized from a variety of biomacromolecules including agarose, albumin, alginate, chitosan, collagen, dextran, fibrin, gelatin, and hylauronan by forming intermolecular crosslinks via thermal or chemical methods[1,2]. Here we demonstrate the ability to form protein hydrogels by a novel non-linear mechanism that begins with an electrostatically triggered partial denaturation of the protein. Partial denaturation increases the protein's hydrophobic surface area, which then drives self-assembly of the protein hydrogel within 10 minutes at physiological temperatures. As an example, we describe the properties of a bovine serum albumin hydrogel formed by this mechanism, although the mechanism is generalizable to other protein species. Atomistic and course-grained molecular dynamics simulations demonstrate electrostatically triggered partial denaturation and hydrogel self-assembly. Gelation at physiological temperatures is demonstrated *in vitro* and rapid post-gelation degradation is shown in a subcutaneous rat model.

1) Peppas, N. A., et al., *Adv Mater* **18**, 1345-1360, 2006
2) Slaughter, B. V., et al., *Adv Mater* **21**, 3307-3329, 2009