

## Technical Proteins: A Multitude of Applications to Discover

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The classical view of proteins is that of hard-working functional entities in the body. Even small mutations in their structures are known to have detrimental effects as their ability to precision target towards for example enzymatic reactions, or signaling is heavily defined by their structural organization [1]. Lately, this understanding has been challenged by the finding that also a class of intrinsically disordered proteins exist in which functionality is rooted in their intrinsic dynamic character [2]. As a result of structural variation, genetic mutations and posttranslational modifications, a multitude of shapes, structures and functionalities arise directly from the overt number of proteins available in nature which are currently being explored as bionanotechnological agents.

Added to its natural presence in many food products, this virtually endless availability of protein functionality, which gives rise to a very wide array of biophysical and chemical properties, in turn resulted into them being exploited in food products. For example, the beer industry heavily relies on proteins for their capacity to provide stable foams [3], while emulsion stabilization exploits the lipid-water interface activity of proteins to provide for their emulsifying properties [4]. With rising understanding of underlying molecular mechanisms, these, and many more applications provided food industry with the perspective of increasing functionality in foods at a relatively low protein concentration. Under processing conditions proteins were found to undergo changes in structure which provided additional means of tweaking protein functionality. For example, heating by means of pasteurization or high pressure processing can lead to denaturation and/or aggregation of proteins [5]. Later it was recognized that food protein functionality can be specifically tuned as the technical application of proteins turned out to result from the presence of a multitude of modifiable groups in the polymeric structure. For example, Maillard reaction induced glycosylation of proteins was found to affect self-assembly tendency [6] while protease assisted hydrolysis was observed to result in improved foaming capacity of proteins from soy, casein and wheat [7]. It is clear from such examples that protein engineering application can lead to even more possibilities to create proteins with different and improved functionalities.

More recently, it has been recognized that the versatility of protein molecules may be of use in other, non-food related and technical applications as diverse as bioadhesives, biomedical applications, drug delivery systems, shampoos and coatings. In terms of biomimicry, the observation that crustaceans secrete multi-protein complexes from a so-called cement gland to aid irreversible underwater attachment [8] is of interest in this respect. Further characterization of these protein complexes lead to the finding that they are often structured as amyloid fibrils [9] rich in cross- $\beta$ -strand structure [9,10]. Typical advantages of using bioadhesives include their biocompatibility for biomedical applications and self-degrading ability. Another recently explored application in the field of biomedical applications is the use of proteins and assembled forms thereof for the preparation of scaffolds and implantations. For example, polycaprolactone/gelatin based nanoscaffolds were effectively used to induce chondrogenesis of induced pluripotent stem cells to enable cartilage tissue engineering [11]. Also in terms of drug delivery the potential of using proteins has been recognized. Gels composed of proteins in an assembled fibrillar

conformation have been reported to be able to act as drug carriers allowing slow-release of small molecules [12].

A typical non-medical application of proteins includes the current recognition that proteins can be assemble into nanowires which can serve a variety of technical applications. The structure of these nanowires is largely based on the so-called amyloid fibril organization of proteins, which has been classically related to a variety of proteinopathies [13]. Molecular dynamics studies of nanowires based on amyloid fibrils composed of human Islet Polypeptide showed that the mechanical behavior of nanowires is a function of the organization of  $\beta$ -sheet structure [14], suggesting that these properties can be tuned. Experimental evidence further showed that the mechanical properties of nanowires composed of amyloid fibrils are controlled by the combined action of fibril sliding and fibril failure and that adhesion strength between fibrils can be manipulated [15]. In addition to this, elastin-based amyloid-like structures [16] and bovine insulin [17] were reported to self-assemble into nanowires with the capacity for electrical conduction.

These examples only touch on the potential that proteins, in assembled state or in the shape of individual molecules, have already shown. The multitude of structures, sizes and the further tunability of structures by means of assembly, engineering and processing reveal that these applications may only present the tip of the iceberg and call for further exploration.

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