# Responsive materials for Biopharma Industry

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## ABSTRACT

Continuous advances in polymer chemistry are enabling the synthesis of novel responsive biomaterials. This class of biomaterials are polymers able to undergo significant changes in their properties in response to external stimuli. Depending on their chemical architecture, responsive polymers can reversibly or irreversibly vary characteristics such as mechanical properties, appearance, structure, viscosity, volume, electrical conductivity, colour, fluorescence, opacity, shape and, ultimately, function.

In the life sciences many of the natural biopolymers, (e.g proteins, polysaccharides, nucleic acids), are themselves natural responsive polymers. Many synthetic polymers are designed to mimic natural biopolymers that exhibit a responsive behaviour to certain environmental stimuli, such as pH, temperature, light, electric fields, ions, enzymes or other molecules. [1].

Among the other "biomimicking" materials, block copolymers and hydrogels are attracting the attention of biopharma industry thanks to their ability to encapsulate, protect and release new biological entitities (NBEs). It is well known that drug delivery systems can increase patient compliance and efficacy of drugs by optimizing their concentration level in the body via either controlled or targeted release. For the biopharm industry drug delivery systems also offer opportunities to differentiate products, rescue drugs that need novel administration, or enhance the patent protenction of the product.

Biotech products such as monoclonal antibodies are powerful disease modifying actives that are also naturally prone to both physical and chemical degradation in host environments. Bioactivty and tolerability are usually related to protein integrity, therefore the protection of a biologic active plays a key role both after administration and during shelf life of the product. Another key potential of drug delivery systems is to enable the administration of NBEs through patient-friendly routes of administration, such as oral or transdermal. As of today, biologics are administered via parenteral route since their bioavailability with other routes of administration is very low (~1%), mainly due to permeation issues.

Some examples of nanostructured responsive materials for the biopharma industry will be shown.

pH responsive hydrogels based on poly(N-2-HydroxyEthyl)-DL-Aspartamide (PHEA-MA) have been synthesized without the use of any toxic reagent via gamma-irradiation [2]. The nanoporosity of hydrogels could be tailored by controlling irradiation parameters, such as total absorbed dose and dose rate, leading to "on-off" release of encapsulated proteins depending on the external pH [3]. The ability of hydrogels to protect the encapsulated protein from harsh conditions, such as highly acidic pH, crowding and high temperatures has also been assessed [3,4].

A "synthetic virus" has been produced that is able to enter cells, escape from the endocytic pathway, and efficiently deliver actives within cells without perturbing their metabolic activity [5]. This biomimetic nanovector is based on the self-assembly of amphiphilic block copolymers into nanometer-sized vesicles (or polymersomes) [6]. The cellular-uptake kinetics can be regulated by controlling the surface chemistry, the polymersome size, and the polymersome surface topology [7]. This latter can be controlled by the extent of polymer phase separation on the outer shell of the polymersome [8].

Finally, "soft" nanocomposites will be presented as candidates for biosensors, based on polyaniline (PANI) nanoparticles finely dispersed into biocompatible hydrogels, able to emit light and conduct electricity depending on pH [9-12].

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