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van Bochove, Bas; Grijpma, Dirk W.; Lendlein, Andreas; Seppälä, Jukka

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Published in:
European Polymer Journal

DOI:
10.1016/j.eurpolymj.2021.110573

Published: 15/07/2021

Document Version
Peer-reviewed accepted author manuscript, also known as Final accepted manuscript or Post-print

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Please cite the original version:
van Bochove, B., Grijpma, D. W., Lendlein, A., & Seppälä, J. (2021). Designing advanced functional polymers for medicine. *European Polymer Journal*, *155*, Article 110573. https://doi.org/10.1016/j.eurpolymj.2021.110573

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Editorial

Designing Advanced Functional Polymers for Medicine

Bas van Bochove[1], Dirk W. Grijpma[2], Andreas Lendlein[3,4] and Jukka V. Seppälä[1*]

[1]Polymer Technology, School of Chemical Engineering, Aalto University, Finland.
[2]Department of Biomaterials Science and Technology, Faculty of Science and Technology, Technical Medical Centre, University of Twente, the Netherlands.
[3]Institute of Active Polymers and Berlin-Brandenburg Center for Regenerative Therapies, Helmholtz-Zentrum Geesthacht, Teltow, Germany.
[4]Institute of Chemistry, University of Potsdam, Potsdam, Germany.
*Corresponding author.

The design of advanced functional polymers for medical applications is a complex process shaped by clinical needs and material structure/function relationships. It spans over multiple scales: macromolecular chemistry and molecular architectures, morphology of polymer matrices, composites materials, as well as complex 3D-geometries on nano-, micro and macroscopic levels. Computational design and subsequent digital fabrication by additive manufacturing are emerging technologies to address this challenge. The study of material/tissue interactions make it a truly multidisciplinary field. Recent developments in these fields, in combination with medical imaging, have created opportunities for personalized medical devices. It is evident that the envisioned multifunctional polymeric biomaterials have a crucial role in achieving future breakthroughs in regenerative medicine, polymeric drug delivery devices, and minimally-invasive surgery.

The selection of polymers for medicine follows has to meet strict requirements. Demands on device mechanics can be translated into molecular structures following structure-property relationships, whether their use is intended for tough load-bearing applications or for implants adapting to pressure-sensitive soft tissues such as neural tissue, they are ideally (bio)degradable and absolutely non-toxic. By developing novel chemistries and equipping existing ones with new functions the materials can be. To that extent, Steinbauer *et al*. synthesized phosphate containing block copolymers to increase the surface adhesion of the materials as phosphorylation is a known adhesion strategy in several species [1]. Arsenie *et al*. enhanced cell adhesion to polylactide (PLA) networks by synthesizing novel networks functionalized with bioactive peptides via the reaction of bifunctional silylated peptides with PLA functionalized triethoxysilyl propyl groups [2]. Izraylit *et al*. also facilitated the incorporation of peptides, by the addition of alkenyl side groups in chain extended PCL [3]. Functionality

can also be used in order to allow high drug loading capacities in polymer matrices by increasing physical interactions. Liang *et al*. created oligopeptides with tailored side-groups of amino acids, which enable such high drug loading [4]. The introduction of low-oxidation-state sulfur atoms can be used to provide macromolecules with responsivity to oxidizing conditions, offering functionality such as bioactivity or targeting. Geven *et al*. review the strategies to introduce these sulfur groups, their responsiveness and biomedical applications [5].

Another method to affect the polymer/property relationships of polymeric devices is by the preparation of copolymers and polymer blends. Careful study of the effects of composition can lead to required breakthroughs. By preparing photo-curable polyurethane copolymers using both PCL and PEG degradation rates and tensile strength were positively adjusted as compared to polyurethane polymers with either PCL or PEG [6]. Alternatively, the mechanical properties can be adjusted by mixing polyesterurethanes and PDLA as shown by Izraylit *et al*. [7]. Blending resulted in stereocomplex crystallites, while crystallization was not observed in PLA alone. By Grijpma and coworkers, two studies investigating blends of GelMA and two- [8] or three-armed [9] PTMC were conducted. For both types of PTMC/GelMA networks, inclusion of GelMA resulted in enhanced mechanical properties and cell adhesion similar to that of 100% GelMA networks. Other approaches described in this special issue include the synthesis and characterization of telechelic macromonomers from CL-co-DX by Fuoco *et al*. [10]. Depending on the composition of CL and DX, amorphous to semi-crystalline oligomer could be prepared. Behl *et al*. developed multiblock copolymers consisting of oligo(caprolactone) of different molecular weights and oligotetrahydrofuran [11]. It was shown that the elongation at break depended on whether the blocks were alternating or random. Cozens *et al*. prepared functionalized PAA polymers, which were crosslinked by different chemistries and mechanisms [12]. Subsequent characterization highlighted the variety of factors responsible for the networks' properties. Dellago *et al*. prepared novel linear cyclic acetal-based monomers for photopolymerizable materials as alternatives to polymers with ester functionalities [13]. These acetals degrade up to 200 times faster than their ester counter parts and the polymer networks showed potential for polymeric biomaterials for bone regeneration.

Porosity has been explored as design parameter on the microscopic level. Grijpma and coworkers report the characterizations of porous crosslinked network films of PTMC [14] and porous PTMC/HA composite scaffolds [15]. Porosity affects the stiffness and toughness of the network films, while the pore size does not appear to have effect. For the composite materials,

not only the stiffness and toughness, but also the surface properties were affected by the porosity. In addition, porosity of the composites influenced the osteogenic differentiation of mesenchymal stem cells with higher porosities resulting in a reduction of calcium production.

Polymer based composites like the ones described above are a highly interesting group of biomaterials due to their excellent physical and mechanical properties. Guo *et al*. review the recent advances in polymer-based composites with regards to selected material components, preparation methods and structure/property relationships [16]. In addition, Toh *et al*. review polymer composites and blends focusing on their application as cardiovascular implants [17].

Designing biomaterials in view of their intended applications is exemplified in several research articles of this special issue. Zhang *et al*. describe mitochondrial structure inspired polymer microspheres based on styrene-butyl-acrylate encapsulating graphene-oxide nanosheets which may find application in as drug delivery devices [18]. Das *et al*. developed a cardiovascular triple layered biomimetic stent prepared from PGA, PCL and PU [19]. Importantly, the PU holds a gallic acid containing anti-oxidant which reduces the migration of vascular smooth muscle cells, thereby potentially decreasing the chance of restenosis. Neffe *et al*. developed a gelatin matrix material that can carry cells which is suitable for *in vitro* test systems and cell-based therapy [20]. Hebels *et al*. developed a micellar system prepared from PEG and poly(*N*-isopropylacrylamide) copolymerized with functional monomers which could be decorated with gold atom clusters [21]. This offers great potential for imaging and diagnostic purposes in biomedical applications.

Hydrogels have great potential for soft tissue engineering purposes. Eshkol-Yogev *et al*. developed composite and nano composite hydrogels, which enhanced the physical and mechanical properties, such as the tensile strength, modulus, gelation time, and swelling degree, of the hydrogels [22]. The composite materials used were montmorillonite and cellulose fibers and they were utilized to prepare hydrogels for novel bio adhesives and medical sealants. Groult *et al*. investigated the effect of the preparation conditions on the structure/property relations of pectin hydrogels [23]. It was shown that by controlling the mode of crosslinking and the drying method drug release could be tailored. Cryogels are hydrogels that are synthesized at sub-zero conditions and have a large, interconnected porous structure. Shiekh *et al*. provide an overview of the recent advancements in design, synthesis and application of cryogels in biomedical applications [24]. In addition, Singh *et al*. describe the

development of polyurethane based nerve conduits with aligned cryogels inside the conduits to make nerve guide channels resulting in improved electrophysiological parameters [25].

The publications gathered in this special issue provide an excellent overview of how polymeric biomaterials are used in the development of novel medical devices. We would like to thank all authors for their contribution and hope you enjoy reading the articles.

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