Designing block copolymer materials

Professor Dr Felix H Schacher describes his passion for macromolecular chemistry and explains how he became interested in the synthesis and application of block copolymers.

What are the applications you have in mind for the block copolymers you prepare?

We use block copolymers for the fabrication of stimuli-responsive membranes – structures where surface polarity, surface charge, pore size and ideally pore selectivity can be manipulated using external stimuli such as pH, temperature and UV light. The materials can be employed in established phase inversion processes and – for amphiphilic materials with hydrophobic and hydrophilic chain segments – process parameters can direct the location of these segments in either matrix or at the pore surface.

In another approach, we focus on block copolymers where one of the blocks can be selectively crosslinked, ideally in a reversible manner. These materials are of interest as ligands for noble metal nanoparticles, as crosslinking prevents ligand exchange and allows for the preparation of hybrid materials with controllable surface properties, or as potential coatings with adjustable hydrophilicity and mechanical properties.

Why are block copolymers particularly attractive as potential self-healing materials?

Polymer chemistry – and, of course, organic chemistry – offers a unique toolbox for equipping materials with different reversible covalent or non-covalent interactions. It can impart structural rearrangements upon external triggers, making it an ideal starting point for the creation of self-healing materials. However, quite often this leads to materials being difficult to process or requiring inconvenient (harsh) conditions. In this respect, block copolymers offer an advantage: by sequentially arranging a segment with self-healing characteristics and another block ensuring solubility or processability, both worlds can be combined. Also, block copolymers undergo microphase separation, allowing nanostructured self-healing materials to be prepared with adjustable domain size and morphology.

Do you collaborate with any other institutions and individual investigators in the pursuit of your research goals?

Of course, many things we work on would not be possible without teamwork. The most important in that respect are local collaborations within the fields of organic/material chemistry, physical chemistry and biotechnology/medicine. In addition, we have many excellent partners within Germany (Karlsruhe, Würzburg, Aachen, Bayreuth), Europe (Moscow, Russia) and Asia (Kyushu, Japan).

Have you faced any particular challenges in your academic career? If so, how did you overcome them?

I started my own research group at the Friedrich Schiller University of Jena, Thuringia, Germany in 2010. In the beginning, the biggest challenge was to quickly establish a functioning network within the University by fostering collaborations and building up the required infrastructure. This would not have been possible without great support from my own institute and other colleagues here in Jena. Another ongoing challenge is to ‘let go’ and give my PhD students enough freedom to make their own experiences and to guide them in developing problem-solving skills.

How important is event attendance to the progress of your research?

Conferences and workshops are essential in terms of disseminating our results and getting to know new colleagues – sometimes also being made aware of recent progress in techniques related to our research. I have to say that I really prefer smaller, topically focused meetings because discussion and exchange is far more intense. I co-organised this year’s biannual meeting of the Macromolecular Chemistry division of the German Chemical Society (GDCh), which was held in Jena on 14-16 September.

Can you explain what initially attracted you to macromolecular chemistry and discuss how your academic background has guided you in this field?

The most important aspects are interdisciplinarity and the possibility to choose and combine different aspects of chemistry. For example, my PhD topic involved organic chemistry, physical chemistry and materials science simultaneously. Of course, this can be the case in other chemistry disciplines as well, but in my opinion this is most pronounced in macromolecular chemistry. In this field, you always operate at the border of other research areas, making it inevitable that you foster strong and reliable collaborations.

In some cases you can perform almost all steps from a bottom-up synthesis to an eventual device on your own: purifying the chemicals; synthesising the (block co-) polymer; characterisation; and finally, assembly into a film, membrane or any other kind of operational device. That, and the fact that my alma mater – the University of Bayreuth in Germany – is particularly strong in polymer and colloidal chemistry, led me to enter the field of macromolecular chemistry.
Stimuli-sensitive structures

Together with partners from different disciplines, a team of polymer chemists at the Friedrich Schiller University of Jena in Germany is completing fundamental studies that focus on exploiting the unique potential of block copolymer materials in a diverse range of applications.

IN RECENT DECADES, macromolecular chemistry has been the birthplace of a variety of promising applications for polymeric materials. Examples range from commercially successful membranes for water purification to the potentially lifesaving prospect of nonviral gene delivery – the latter is still under intense investigation. Indeed, with block copolymers in particular, it can be expected that the scope of applicability has yet to plateau.

This is largely due to the unique possibility of block copolymers to combine different properties (hard, soft, elastic, stiff, hydrophilic, hydrophobic, etc.) within a single material and create nanostructured materials via self-assembly processes. As this can be exploited in solutions, thin films, the bulk state or within porous structures, numerous combinations can be imagined. As a result, scientists are paying increasing attention to such materials in diverse application fields, ranging from biomedicine to physics, materials science and biotechnology.

POLYMER SYNTHESIS AS FUNDAMENT

In many of these endeavours, the unique opportunities afforded by block copolymers join with a range of difficulties regarding proper and selective functionalisation, unknown cytotoxicity, and the need for scalable and robust manufacturing processes. This might well mean that working on untrodden ground involves processes and assembly steps that are simply not yet fully understood.

Dr Felix Schacher is Junior Professor at the Friedrich Schiller University of Jena, where he has led a research group focusing on creating and manipulating nanostructured polymeric materials since 2010. As part of the Laboratory of Organic and Macromolecular Chemistry and the Jena Centre for Soft Matter, the research of Schacher’s group is a highly collaborative affair poised at the intersection of many different fields.

Primarily, Schacher conducts studies into the synthesis, self-assembly and application of polymeric materials at length scales ranging from the nanometre to the micrometre. "To a certain extent, polymer chemists are control freaks," Schacher muses. His goal is to control precisely how many functional groups are present in a material, where they are located and how they can be selectively addressed. From conventional free radical to ‘living’ ionic methods of polymerisation, these studies implement a range of techniques in order to synthesise and characterise functional polymers and block copolymers.

CHALLENGES FOR SAFE DELIVERY

Recently, important strides have been taken in the field of nanomedicine where the exploitation of block copolymers could herald in an innovative new approach to treating a range of chronic diseases, such as immune defects and cancers.

To carry out successful nonviral gene delivery, the protection of nucleic acids is required while simultaneously maintaining the maximum biocompatibility of the polymeric material as it is delivered alongside the genetic material into eukaryotic cells.

Currently, the gold standard for in vitro applications that best achieves these ends is the cationic polymer polyethylenimine. Unfortunately, if polymeric systems reach a high transfection efficiency, levels of cytotoxicity also increase and undermine the effectiveness of the method. Furthermore, techniques designed to reduce cytotoxicity are not sufficiently discriminatory and reduce transfection efficiency along with it.

Targeting immune cells causes its own considerable obstacles. Unlike adherent solid tissue cells, immune cells are suspended in the bloodstream. Transferring genes into suspension cells is far trickier and usually leads to failure, largely because the likelihood of contact between suspension cells and DNA-polymer combinations—polyplexes—is reduced by 3D cell cultivation.

UNDERSTANDING PARTICLE-CELL INTERACTIONS

Schacher’s research, alongside partners in biotechnology and medicine, has been instrumental in turning this situation around. The ability to synthesise and manipulate nanometre-scale polymeric objects sensitive to environmental stimuli has directly led to a promising agent to transfect plasmid DNA (pDNA) into different cell lines, including human leukaemia cells. Exploiting the properties of stimuli-responsive building blocks to change size, shape, polarity or charge, Schacher formed multi-responsive micelles with a patchy surface from triblock terpolymers – he arranged materials with three chemically different monomers in a sequential manner. When these particles experienced a pH range of 5.5-7.4, both the shell and corona underwent...
structural rearrangements that allowed an unprecedented rate of cellular uptake into leukaemia cells and subsequent release of pDNA.

Compared with the state-of-the-art polymeric systems, this new approach to nonviral gene delivery combined remarkably high transfection efficiency with low cytotoxicity in both adherent and suspension cells. One possible cause for such enhanced performance is the sequential arrangement of two oppositely charged weak polyelectrolytes in the original material. “We think that the presence of a competing polyanion is responsible for both the improved release of pDNA and the comparatively low cytotoxicity,” Schacher explains.

Considering that very little is known about the causal mechanisms of transfection for pDNA, Schacher’s results represent a vital contribution towards its comprehension. However, this was just the first step; although this system seems to be chemically understood, many questions regarding the individual steps during uptake, release and degradation still need to be answered. Nevertheless, a profound understanding of transfection into immune cells might improve future treatments for HIV and leukaemia.

MATERIALS WITH INTRINSIC DYNAMICS

A particularly exciting area in polymer chemistry today is the drive to produce materials featuring reversible chemical bonds. This imparts certain ‘dynamics’ and can be used to generate, for example, self-healing materials. In that respect, polymer chemistry is attractive because of its ability to equip materials with reversible covalent or non-covalent interactions, it provides the perfect conditions for addressing this issue. Schacher’s research has produced one of the first examples of a self-healing material based on block copolymers. The advantage of this approach is that the blocks ensure processability. Indeed, Schacher’s studies have led to nanostructured materials with feature sizes in the range of 15-20 nm that are capable of reversible crosslinking and decrosslinking. Despite still requiring long cycle times of several hours and high temperatures, a proof-of-concept has been made and this will be further exploited in the framework of a German Research Foundation (DFG) priority programme (SPP1568) on self-healing materials.

In another project involving similar chemistry, his group focuses on hybrid nanoparticles with a gold core and a block copolymer ligand shell – the latter can be reversibly crosslinked. In that way, ligand mobility and, ultimately, surface characteristics and solubility of such materials can be precisely adjusted. Schacher is sure that this will also affect biocompatibility and the interaction with soft matter in general – situations where competitive ligands might be present and – without crosslinking and ‘locking’ of the status quo – changes in the ligand shell can drastically alter material characteristics.

RESPONSIVE POROSITY

Among the group’s range of activities, Schacher has found ample time to apply his expertise in stimuli-responsive polymeric systems to a more traditional focal point of polymer chemistry – membranes. Although it is unlikely that the block copolymer membranes designed in his lab will garner the commercial success of existing membrane materials like polyethersulfones, Schacher’s materials might have the edge where selectivity is concerned. For example, in reaction to pH, temperature or UV light, a stimuli-responsive membrane can separate nanoparticle or protein mixtures according to size or charge. However, unique selling points do not equal finished products: “Something that is continually on my mind is establishing pore size control in membrane materials by mechanical force,” Schacher states. Features such as these may lend themselves to advanced filtration methods and thereby the removal of contaminants from water or food sources, but these areas have yet to be explored.

Pressing firmly on with non-viral gene delivery, membranes, self-healing systems and an array of other projects, Schacher is expecting that over the coming decade his lab will have contributed to a more profound understanding of the interactions between multifunctional macromolecular assemblies and biological matter.

What’s next?

• To understand the influence of charge and charge distribution on particle-cell interactions (uptake and cytotoxicity)
• To complement our existing toolbox for controlling amount and type of functional groups on particle surfaces and within nanostructured films
• To develop membrane solutions for separation according to charge or surface chemistry

INTELLIGENCE

CREATING AND MANIPULATING NANOstructured MATERIALS

OBJECTIVES

• To synthesise and characterise innovative multifunctional polymers and block copolymers
• To increase predictability and control in the self-assembly of polymers and block copolymers at different length scales
• To exploit the benefits of block copolymers in different applications

TEAM MEMBERS

For a full list of team members, please visit: www.jenano.de/Members.html

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FUNDING

German Research Foundation (DFG) • German Ministry for Education and Science (BMBF) • German Ministry for Economy (BMWi) • Thuringian Ministry for Science, Education and Culture (TMWK) • Carl Zeiss Foundation • German Chemical Industry Association (VCI) • German Academic Exchange Service (DAAD)

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