EDITORIAL
Peptoids in Wonderland
Kent Kirshenbaum and Ronald N. Zuckermann, Biopolymers 2019, doi: 10.1002/bip.23279

REVIEW
Design and preparation of organic nanomaterials using self-assembled peptoids
Alessia Battigelli, Biopolymers 2019, doi: 10.1002/bip.23265

FULL PAPERS
Dual-responsive pegylated polypeptoids with tunable cloud point temperatures
Xiaohui Fu, Jiliang Tian, Zheng Li, Jing Sun and Zhibo Li, Biopolymers 2019, doi: 10.1002/bip.23243

Solid-phase synthesis of three-armed star-shaped peptoids and their hierarchical self-assembly

Polymerization rate difference of N-alkyl glycine NCAs: Steric hindrance or not?
Tianwen Bai and Jun Ling, Biopolymers 2019, doi: 10.1002/bip.23261

Linking two worlds in polymer chemistry: The influence of block uniformity and dispersity in amphiphilic block copolypeptoids on their self-assembly
Niklas Gangloff, Marcel Höferth, Vladimir Stepanenko, Benedikt Sochor, Bernhard Schummer, Joachim Nickel, Heike Walles, Randolf Hanke, Frank Würthner, Ronald N. Zuckermann and Robert Luxenhofer, Biopolymers 2019, doi: 10.1002/bip.23259

Peptoids advance multidisciplinary research and undergraduate education in parallel: Sequence effects on conformation and lipid interactions

Phosphoramitoids—A submonomer approach to sequence defined N-substituted phosphoramidate polymers
Thomas Horn, Michael D. Connolly and Ronald N. Zuckermann, Biopolymers 2019, doi: 10.1002/bip.23268

Solution effects on the self-association of a water-soluble peptoid
A facile on-bead method for fully symmetric tetra-substituted DOTA derivatizations using peptoid moieties

Macrocyclization enhances affinity of chemokine-binding peptoids
Peptoids in Wonderland

Straddling the iconic disciplines of Structural Biology and Polymer Science lies a newly emerging field—Bioinspired Polymers. With the discovery of innovative polymers that are chemically diverse in sequence, structurally tunable and biocompatible, chemists have long dreamed of creating new materials that bridge the gap between synthetic polymers and biomacromolecules. Such materials will certainly find broad utility in many exciting areas, ranging from biomedicine to nanotechnology, and the great promise of bioinspired polymers is increasingly attracting additional investigators. However, the field faces fundamental limitations: in order to be a truly impactful discovery platform, the materials need to be readily synthesized and their molecular structures reliably controlled. Peptoids, or poly-N-substituted glycines, with almost three decades of fundamental research behind them, are well-positioned to overcome these limitations.

Indeed, rather fortunately, one of the most compelling attributes of peptoids is their synthetic efficiency and versatility. Iterative solid-phase sub-monomer synthesis allows for precise sequence control of oligomers and short polymers, and the living solution polymerization of N-carboxyanhydrides provides access to high molecular weight polymers. Both these synthetic routes enable the generation of tremendous chemical diversity within the side chain substituents, deriving from the ready availability of hundreds of inexpensive primary amine synthons. Peptoid synthetic methods thus provide rapid, practical and scalable routes to a highly designable and diverse class of materials. The low-costs, high-yields and reliable protocols are enabling researchers from many fields to explore peptoids across a broad range of disciplines. The yellow-brick road to a largely unexplored peptoid Wonderland has now been paved, and parties of intrepid researchers can readily investigate what lies beyond.

To celebrate the extensive range of science enabled by these advances in sequence-controlled polymers, we have assembled a collection of articles for this special issue of *Biopolymers* from a variety of active investigators in the peptoid field. The great response from the research community means these articles will be published across two issues of the journal. In this issue, Part 1, it is evident that peptoids are being tailored to make critical advances in nanomaterials, diagnostics and therapeutics.

The issue begins with a review by Battigelli, discussing recent advances in the design, mechanism of formation and application of self-assembled peptoid nanomaterials. The first two primary research articles, by Fu et al. and Jin et al., continue the theme, exploring the ability of amphiphilic peptoids to self-assemble into well-defined nanomaterials.

In these examples, the peptoid portions of the structures are tuned to reveal subtle relationships between monomer sequence and the supramolecular structure.

Bai and Ling use density functional theory calculations to glean insight into the effects of monomer solubility and steric hindrance on chemical reactivity in solution polymerization of several N-substituted N-carboxyanhydrides. In their article, Gangloff et al. take a pioneering look at the largely unexplored boundary between monodispersity and polydispersity in polymer science. The study probes the very intersection of the polymer and biopolymer worlds by examining the impact of chain length heterogeneity on the morphology and physical properties of block copolypeptoid assemblies. It is the versatility of peptoid synthesis that allows fundamental questions like this to be addressed for the first time within the same system.

The simplicity of the sub-monomer method makes it easily accessible to non-experts, and the contribution from Jimenez et al. describes how the chemistry can be used as part of a teaching module in the undergraduate organic chemistry laboratory. Horn et al. take the unusual step of applying the sub-monomer philosophy to a new class of sequence-defined polymers based on an N-substituted phosphoramidate backbone. Like peptoids, these oligomers are made from a diverse set of amine submonomers and use simple, cheap reagents. The so-called “phosphoramitoids” have an interesting blend of properties reminiscent of both nucleic acids and proteins, and could lead to an exciting new class of biomimetic oligomer. Fuller et al. probe the ability of sequence-defined amphiphilic peptoid helices to self-associate into protein-like bundles. The results shed light on a most important goal of the field: to mimic the folded architecture (and function) of a protein domain. Rustagi and Udugamasooriya, and Brahm et al. round out the issue by exploring the combinatorial discovery of biologically active peptoids. The former report a facile synthesis of metal-chelating peptoids to serve as new bioimaging reagents, while the latter describe the screening of peptoid macrocycles with the goal of combating inflammatory disease.

The exciting body of work in this collection nicely illustrates how a single class of material can have an impact on several different areas of science. We anticipate these studies will increase interest in the field and attract new researchers with problems that might be solved using polypeptoids. As more investigators realize just how easy peptoids are to make, and how precisely their structures can be controlled, we hope
that scientists from many disciplines join. The peptoid yellow-brick road is ready to welcome the next generation of researchers to venture into new realms of creativity and wonder.

Kent Kirshenbaum
Department of Chemistry
New York University
New York, U.S.A.

Ronald N. Zuckermann
The Molecular Foundry
Lawrence Berkeley National Laboratory
Berkeley, U.S.A.