Discussion on “Aperiodic Copolymers”

Stuart J. Rowan, a Christopher Barner-Kowollik, b Bert Klumperman, c Pierre Gaspard, d Robert B. Grubbs, e Marc A. Hillmyer, f Lian R. Hutchings, g Mahesh K. Mahanthappa, h Rachel K. O’Reilly, i Makoto Ouchi, j Mitsuo Sawamoto, k Timothy P. Lodge l

a Department of Macromolecular Science and Engineering, Case Western Reserve University, 2100 Adelbert Road, Cleveland OH 44106, USA; b Preparative Macromolecular Chemistry, Institut für Technische Chemie und Polymerchemie, Karlsruhe Institute of Technology (KIT), Engesserstr. 18, 76128 Karlsruhe, Germany; c Department of Chemistry and Polymer Science, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa; d Centre for Nonlinear Phenomena and Complex Systems, Université Libre de Bruxelles (ULB), Campus Plaine Code Postal 231, B-1050 Brussels, Belgium; e Chemistry Department, Stony Brook University, Stony Brook NY 11794-3400; f Department of Chemistry, University of Minnesota, 207 Pleasant Street SE, Minneapolis, MN 55455; g Developmental Programs, Institut für Technische Chemie und Polymerchemie, Karlsruhe Institute of Technology (KIT), Engesserstr. 18, 76128 Karlsruhe, Germany; h Department of Chemistry and Polymer Science, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa. i Centre for Nonlinear Phenomena and Complex Systems, Université Libre de Bruxelles (ULB), Campus Plaine Code Postal 231, B-1050 Brussels, Belgium; j Chemistry Department, Stony Brook University, Stony Brook NY 11794-3400. k Department of Chemistry, University of Minnesota, 207 Pleasant Street SE, Minneapolis, MN 55455; l Department of Chemical Engineering & Materials Science, University of Minnesota, 421 Washington Ave. SE, Minneapolis, MN 55455; m Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan.

ABSTRACT: In a recent Viewpoint (ACS Macro Lett. 2014, 3, 1020), J.-F. Lutz brought to the community’s attention the need for more informative nomenclature, especially with respect to macromolecules with prescribed but not repeating sequences of monomers. Lutz proposes the use of the term “aperiodic” for this situation. In this Viewpoint, we comment on the need for such nomenclature, and offer some alternatives for consideration.

Accessing sequence specificity in synthetic polymers, with the same level of sequence control as peptides or nucleic acids, has been a “Holy Grail” for polymer scientists since the early days of the field. While this has yet to be achieved in high molecular weight synthetic polymers, there have been some significant developments in polymer chemistry that have sparked a growing interest and a resurgence in this field. One of the significant developments in polymer chemistry that have naturally arisen is the need for more informative nomenclature, especially with respect to macromolecules with prescribed but not repeating sequences of monomers. Lutz proposed the use of the term “aperiodic” for this situation. In this Viewpoint, we comment on the need for such nomenclature, and offer some alternatives for consideration.

Lutz goes on to give examples (Figure 2) of Aperiodic Copolymers. These include multiblock copolymers whose block sequence is aperiodic, multisite copolymers with different repeat units that are aperiodically distributed along a homopolymer backbone, and sequence-defined copolymers without regular repeating sequences (akin to what is seen in most proteins and DNA).

Figure 1. Schematic (taken from the Lutz Viewpoint) showing the relationship of selected official (blue) and unofficial (gray) to the new proposed terminology (red) that can be used to classify synthetic copolymers.
Scientific terminology can be a sensitive topic, and intriguing by this Viewpoint, the Editors thought it would be interesting to elicit comments from the members of the community on the proposed use of the term aperiodic copolymers. The following distills and summarizes the comments received from the authors of this Viewpoint. Two broad conclusions emerge from the individual comments received. First, there was general agreement that current terminology is not adequate to describe the kinds of macromolecular structures that are synthetically accessible, and that Lutz has done the community a service by bringing up such an important point. Second, however, there was near unanimity that “aperiodic” is not the ideal term to describe the structures that Lutz considers. This is due to the fact that the term “aperiodic” is really stressing what the target polymer structure is not, rather than what it is. To many, “aperiodic” carries a strong implication of “irregular” or even “random”, which is the opposite of what the term wishes to convey in this context. While, “aperiodic” does not require the notion of randomness, it is nevertheless associated with it in everyday use by many, which was confirmed by a questioning of a (non-representative) series of colleagues, PhD students and post-doctoral fellows.

As such, the term aperiodic copolymer was viewed as being too broad to describe the sort of copolymers that Lutz wishes to define. Nonetheless, Lutz is correct in pointing out that a population of information-containing copolymers (such as the interesting and synthetically challenging structures shown on the right hand side of Figure 2) should differ from a population of statistical copolymers, even though the individual copolymers of both populations have sequences without apparent regularity. Such a differentiation can have important implications, for example, in DNA replication.

In seeking suitable nomenclature, some generally desirable principles emerge. These include: (i) name things by what they are (or strive to be), rather than what they are not; (ii) aim for simplicity and minimal ambiguity; (iii) favor shorter terms when the meaning is clear from the context, but allow for increased specificity when needed; (iv) for synthetic polymers, with their inherent probability of heterogeneity within a population, tolerate modest deviations from the ideal. Accordingly, it seems to us that the terms “sequence-specific” or “sequence-defined” would cover the intention of “aperiodic”. From a synthetic perspective, controlling sequence is the critical question and is a separate issue from periodicity—whether the resulting polymer structure is aperiodic, periodic, gradient, etc., is secondary. As such the descriptor “sequenced” might be more versatile, especially if the level at which the sequencing occurred could be specified: “monomer-sequenced”, “block-sequenced”, (and perhaps “functional group or functionality-sequenced,” though there may well be a better term to be found for this concept).

When it comes to multiblock copolymers (Figure 2 left) the complexity of the matter can further be highlighted by an example that Lutz provides on a multiblock ABCABCABC polymer (where A, B and C represent different homopolymer segments), which can be considered as a periodic polymer with an (ABC) structure. However, this does not say anything about the individual block lengths. Are all blocks of the same chemical composition identical in chain length? If they are not, the degree of periodicity significantly decreases and a more complex description is necessary to precisely describe the polymer. This could be addressed by expanding to “block-sequenced-specific” or “block-sequenced-defined”, and the right side of Figure 2 correspondingly with “monomer-sequence-specific” or “monomer-sequence-defined”.

One apparent shortcoming of this proposed terminology is a failure to distinguish between structures with repeating sequences and those without, and this gets to the heart of Lutz’s proposed nomenclature. However, it is an interesting question, whether the crucial distinction is really between presence or absence of repetition, or rather whether it is between structures in which the identity of the monomer at every position along the chain is prescribed, or not. We suspect it is the latter dichotomy that is ultimately of more interest. Nevertheless, the proposed nomenclature could be expanded if needed, for example to “aperiodic-monomer-sequence-defined” and “periodic-monomer-sequence-defined”. Although bordering on the cumbersome, these terms are unambiguous.

Another possible shortcoming of the above proposed nomenclature is the fact that alternating copolymers, or even homopolymers, could claim to be “monomer-sequence-defined”. However, context is everything. No-one would be fooled into believing that an alternating copolymer was some...

---

**Figure 2.** Schematic representation, proposed by Lutz, of different types of aperiodic copolymers: multiblock copolymers (left), multisite copolymers obtained using time-controlled monomer additions (middle), and monodisperse sequence-defined copolymers (right).
how more “sophisticated”, because it was given the appellation “sequence-defined”. Indeed, abababababababababababababababab (where a and b represent different repeat units here) is a sequence, it is just a trivial (and periodic) one. An analogy to number theory might be apt: the fact that 2 and 3 are prime numbers, but of little use in applications where larger prime numbers are important, does not diminish the richness of the general theory of prime numbers.

The proposed nomenclature does not yet provide a unique identifier for the case of multisite polymers illustrated in the middle of Figure 2. Accordingly, possibilities include “intermittent-site-specific”, “site controlled” (although, it is worth pointing out here that “site controlled” already has a specific meaning in catalysis and site vs chain-end control is important terminology in catalyzed coordination polymerizations so one has to be careful with the use of this term) or “site-sequenced”.

The bottom line is that Lutz is right: IUPAC nomenclature is inapplicable to some complex structures out there and in particular those that show no periodicity. This leaves a situation where researchers working on polymers with a more defined non-periodic sequence than a random copolymer but less precise than a protein have struggled to describe their materials in less than one line. Most publications highlight the potential of their systems by referring to them as “sequence-controlled” polymers, although a truly controlled sequence is hardly ever the case. In other cases, authors of papers describing such polymers have skillfully avoided naming the polymers per se, and instead describe the process of their syntheses as “programmed”, “sequential”, etc. In the case of multiblock copolymers the nomenclature seems to be straightforward, with a Greek-derived descriptor prefix (di, tri, tetra...trideca, etc) followed by the word “block”. However, where the degree of polymerization (DP) of the respective blocks decreases to only a few repeat units, the resulting polymer will surely lack the properties of a multiblock copolymer (i.e. phase separation, compartmentalization, etc.) and be more similar to a statistical copolymer. The proposed "aperiodic" terminology is interesting but from our very small, unscientific survey, appears not to capture the ideal of a non-periodic sequence-defined synthetic polymer. In this discussion we have suggested alternatives with the realization that exceptions still arise. It may for example, be necessary to find separate definitions for certain classes of polymers discussed herein. One example could be to have different terms for multi-block polymers vs other copolymers. Indeed, Lutz acknowledges that the terminology of block copolymers has evolved in parallel to that of other copolymers wherein the local sequence distribution variations occur at the length scale of a single monomer unit.

In any event, we intend that this discussion along with a set of alternative terms as discussed above, will help to promote dialogue so as to achieve consensus among researchers in the field and even to inspire more in-depth and innovative research in this challenging and exciting segment of polymer science.

**AUTHOR INFORMATION**

**Corresponding Author**

*stuart.rowan@case.edu* (SJR); *lodge@umn.edu* (TPL)

**ACKNOWLEDGMENT**

The authors would like to thanks J.F. Lutz for putting forward the original Viewpoint and being supportive of the idea of this follow-on community discussion. RKO would like to thank Dafni Moatsou for discussions.

**REFERENCES**

3. Hess, M.; Kitayama, T.; Metanomski, W. V.

**Graphical Abstract**