

University of Groningen

## Structure-Function Relationships in Dynamic Combinatorial Libraries

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DOI:  
[10.33612/diss.90038152](https://doi.org/10.33612/diss.90038152)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Altay, M. (2019). *Structure-Function Relationships in Dynamic Combinatorial Libraries*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.90038152>

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## Chapter 6

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# Conclusion and Perspectives

**D**ynamic combinatorial and supramolecular chemistry are two emerging fields in chemistry in which complex systems arise from simple precursors. With a bottom-up approach in this field, scientists are capable of addressing questions related to the origins of life and de-novo life research by mimicking biochemical processes occurring in living systems. This thesis is focused on the development of new replicating systems, based on multiple building blocks featuring relatively small structural variations. In order to develop such systems, it is important first to understand what is ‘living’ and through which features ‘living’ differs from ‘non-living’. In **Chapter 1**, we discuss this issue by addressing some of the most plausible definitions of life and fundamental features of living systems. Although there is still no consensus of the exact definition of ‘life’, the best we can do is to take most working definitions as reference and try to design complex molecular networks accordingly.

Inspired by living polymerization, which is a very common process used in material science, our group recently demonstrated that self-replication and self-assembly can be used to produce supramolecular polymers with controllable growth and length.<sup>1</sup> In **Chapter 2**, we reported kinetically controlled synthesis of supramolecular block copolymers by using seeds made from another building block which were shortened by using a Couette cell. Experimental findings showed that the morphology of the sheared seeds has a strong effect on the final composition of the fibers. In such systems, understanding the fiber growth mechanism is challenging and requires careful analysis of the nature of the seed fibers and the effect of shearing. Additionally, as the two building blocks are structurally very similar, the corresponding fibers have very similar diameters and contrast. This complicates visualization of the block cofibers by microscopy. In order to tackle this issue, we worked on directly visualizing the block cofibers by introducing halogens into the building block. Fibers formed from novel halogenated building blocks showed that, for a detailed electron mapping of the small assemblies, a higher density of halogens is required. Thus, building block design requires improvement. If building blocks with sufficient contrasts can be utilized in block cofiber synthesis, imaging can be performed without stains containing heavy metal salts, which would decrease the background noise in microscopy images.

In biology, mutations occur when self-replication does not produce a perfect copy of the information to be inherited. As a result, new species can emerge and are subject to natural selection, where species that are better adapted to the environment survive. In **Chapter 3**, small mutations were introduced into two different building blocks and their self-replication behavior was studied in various environments. While in one case mutants formed differently sized self-replicators depending on the environment, in another case self-replication was completely inhibited. The results show that life-like processes can be observed in dynamic molecular systems but also show that there is still a lot to explore and develop, before we reach the goal of the de-novo synthesis

of life.

In **Chapter 4**, we aimed to mimic, and possibly explore, new life-like features in a dynamic molecular system that starts from a single self-replicator and evolves into a more complex multi-replicator system. We discovered features analogous to biological systems: parasitic and partially predatory behavior between replicating molecules.<sup>2</sup> We reported the emergence of a new class of 6-ring replicators by consuming a pre-existing 8-ring replicator. Moreover, the fact that only the 8-ring replicator is capable of cross-catalyzing the formation of 6-ring replicators (but not vice versa) reveals a non-mutualistic behavior between the self-replicators. Although the system still lacks of some other important features of living systems, like compartmentalization and metabolism, an important step in the creation of complex multi-replicator systems was demonstrated.

Living systems are complex machineries that are maintained by out-of-equilibrium processes which operate with high efficiency. We attempted to build an out-of-equilibrium system to study the evolution of species by infusing nutrients with varying composition and simultaneously withdrawing material at a constant rate in a continuous flow setup. By doing so, we aimed to construct a dynamic cross-catalytic pathway which produces new species that cannot cross-catalyze the original replicator. Such dynamic environment was shown to induce diversification of species when two different building blocks are involved. However, producing such a cross-catalytic pathway also requires careful analysis as the number and type of species in the DCL becomes more diverse over time. We believe that investigating such dynamic systems in continuous flow regimes may lead to the emergence of new replicators sets under out-of-equilibrium conditions. Evolution of such systems will hopefully create new opportunities to study more diverse systems than we can access today.

In aiming for expanding scientific knowledge, supramolecular and dynamic combinatorial chemistry are two very useful tools as they let to study some of the most intriguing questions in fundamental research. Hopefully, in the future, separate independently studied features of living-systems will be integrated into single multi-functional living entities.



## 6.1 References

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