



The Pappas research group is offering the following position:

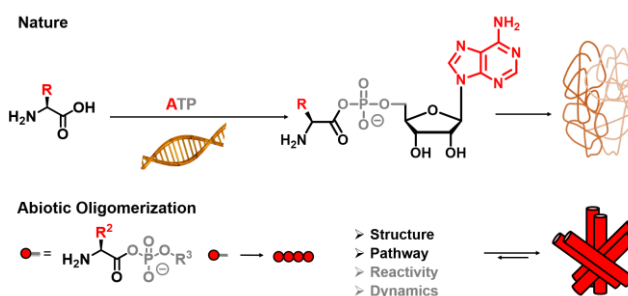
ERC-funded PhD position: **Departing from Randomness: Constructing Multifunctional Reaction Networks with Aminoacyl Phosphate Esters**

More information about our research focus: <https://pappasresearchgroup.com/>

Starting date: 01/05/2025 or earliest possible time

### Project description

Phosphates and phosphate esters are the cornerstone of molecular organization in biological systems, driving processes such as genetic encoding, signal transduction, and chemical energy transfer. These highly versatile molecules act as both structural frameworks and energetic drivers, facilitating complex biochemical processes that sustain life. Beyond their biological roles, phosphates offer a fascinating platform for designing synthetic chemical networks, capable of mimicking or even surpassing natural systems in complexity and functionality. Inspired by these natural paradigms, this project seeks to depart from randomness by leveraging the unique properties of aminoacyl phosphate esters<sup>1-4</sup> to encode selectivity and introduce



**Fig. 1.** Enzyme-free amino acid oligomerization using aminoacyl phosphate esters.

structure into multicomponent reaction networks (Fig. 1). It will explore how dynamically controlled oligomerization can yield well-defined assemblies incorporating peptides, sugars, nucleobases, and other building blocks, driven by phosphate fuels and substrates. The key aims of the project are to (i) synthesize aminoacyl phosphate esters composed of different compound classes (ii) investigate how mixtures of activated building blocks can be channeled to yield defined oligomers both in and out of equilibrium and (ii) characterize these systems in terms of composition, nanoscale architecture and supramolecular interactions. A central focus will be to understand the chemical design space for the structural behavior of aminoacyl phosphate esters. This will involve systematic exploration of variations in side chains, N-terminal functionalities, and phosphate ester modifications. These structural variations are expected to direct distinct pathways by transferring energy and reactivity to drive the formation and destruction of assemblies. Incorporating structural elements around non-biological phosphates represents an unexplored frontier in phosphate-driven supramolecular systems chemistry, offering new opportunities to develop dynamic and multifunctional reaction networks.

### Relevant publications

1. Dai, K.; Pol, M.; Saile, L.; Sharma, A.; Liu, B.; Thomann, R.; Trefs, J.; Qiu, D.; Moser, S.; Wiesler, S.; Balzer, B.; Hugel, T.; Jessen, H.; Pappas, C. G., Spontaneous and Selective Peptide Elongation in Water Driven by Aminoacyl Phosphate Esters and Phase Changes. *J. Am. Chem. Soc.* **2023**, 145, 48, 26086–26094.
2. Pol, M.; Dai, K.; Thomann, R.; Moser, Pappas, C. G., Guiding Transient Peptide Assemblies with Structural Elements Around Abiotic Phosphate Fuels. *Angew. Chem. Int. Ed.*, **2024**, e 202404360.
3. Pol, M. D.; Thomann, R.; Thomann, Y.; Pappas, C. G. Abiotic Acyl Transfer Cascades Driven by Aminoacyl Phosphate Esters and Self-Assembly. *J. Am. Chem. Soc.* **2024**, 146, 29621–29629.
4. Sharma, A.; Dai, K.; Pol, M. D.; Thomann, R.; Thomann, Y.; Roy, S. K.; Pappas, C. G. Selective Peptide Bond Formation via Side Chain Reactivity and Self-Assembly of Abiotic Phosphates, *in press*.

### Candidate profile

For this project interdisciplinary competences ranging from organic and analytical chemistry to supramolecular are desirable. The potential PhD candidates are therefore expected to have a master degree with outstanding grades in one of the following fields (chemistry, polymer science, functional materials) and the strong willingness to work interdisciplinary. Previous experience in one of the following areas (solid and solution phase peptide synthesis, dynamic covalent chemistry, spectroscopic techniques) is appreciated, but it is not a requirement. In addition, strong competences in scientific presentations and writing (in English language) as well as team skills are expected from the successful PhD candidate as they will be part of a creative, productive and dynamic research team.

### Please hand in:

- **Motivation letter detailing why you are interested in this specific project, what potential ideas you could develop** and how your previous research qualifies you for the project (up to 1,500 words)
- Curriculum Vitae with list of publications (if applicable)
- Certified copies of your university degree(s) with grades (BA and MA certificate / Diploma certificate and transcript)
- Short summary of your master's thesis (up to 1,000 words)
- Two reference letters

This position is for 36 months. The salary will be determined in accordance with TV-L E13.

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Please send your application in English including supporting documents mentioned above by 03/20/2025 at the latest. Please send your application to the following email address:

**Contact person about position:**

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