

Title	Towards active matter: Driving chemical systems away from equilibrium
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International Secondment	
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PI	Prof. Jurriaan Huskens
Institute	University of Twente
Place, country	Enschede, Netherlands
# months (min.3)	=>3 months

Project description:

Life is a non-equilibrium state of matter maintained at the expense of energy. As energy source, nature uses predominantly chemical energy stored in thermodynamically activated, but kinetically stable, molecules. These high-energy molecules are exploited for the synthesis of other biomolecules, for the activation of biological machinery such as pumps and motors, and for the maintenance of structural order. Knowledge of how chemical energy is transferred to biochemical processes is essential for the development of synthetic active matter.

The development of synthetic active matter requires the ability to design materials capable of harnessing energy from a source to carry out work. Nature achieves this using chemical reaction cycles in which energy released from an exergonic chemical reaction is used to drive biochemical processes (Figure 1). Although many chemically fuelled synthetic reaction cycles that control transient responses, such as self-assembly, have been reported, the generally high complexity of the reported systems hampers a full understanding of how the available chemical energy is actually exploited by these systems. This lack of understanding is a limiting factor in the design of chemically fuelled active matter.

In a joined publication, the Prins- and Frezzato-groups have recently reported a minimalistic chemical reaction network that produces a hydrazone using adenosine diphosphate (ADP) as a chemical fuel. The addition of ADP to a mixture of functionalized aldehyde and hydrazide results in the accelerated formation of a hydrazone product that turns out to be a catalyst for the hydrolysis of ADP into AMP and P_i that is better than the reactants. In other words, ADP drives the formation of a catalyst for its own destruction. The minimalistic nature of this network, especially compared to natural equivalents, permitted a determination of all kinetic and thermodynamic parameters (i.e. rate and binding constants for all reactions and chemical equilibria occurring in the network). Kinetic models were

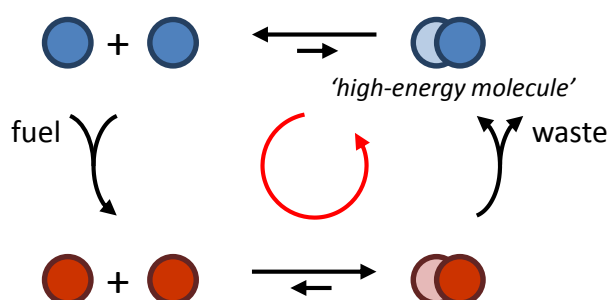


Figure 1. Schematic representation of the fuel-driven synthesis of an activated molecule.

built that provided an insight on how energy released from ADP hydrolysis was exploited and, importantly, provided insights in the design of future chemical reaction networks.

This project aims at exploiting the acquired knowledge for the design of new chemical reaction cycles in which turnover rate, precision and energy dissipation can be controlled.

Skills that will be acquired:

Organic chemistry: synthesis and characterization of organic molecules

Supramolecular chemistry: determination of binding constants and rate constants

Physical-organic chemistry: development of thermodynamic and kinetic models

Physical chemistry: concepts of non-equilibrium chemistry

International secondment:

The secondment will be carried out in the group of prof. Jurriaan Huskens (University of Twente, Netherlands) and will be dedicated to the determination of binding and rate constants using a variety of techniques (spectroscopies, ITC, ...).

References:

1. Ragazzon, G.; Prins, L. J. Energy Consumption in Chemical Fuel-Driven Self-Assembly. *Nat. Nanotechnol.* **2018**, *13*, 882–889.
2. Das, K.; Gabrielli, L.; Prins, L. J. Chemically Fueled Self-Assembly in Biology and Chemistry. *Angew. Chem. Int. Ed.* **2021**, *60*, 20120-20143.
3. Marchetti, T.; Frezzato, D.; Gabrielli, L.; Prins, L.J. ATP Drives the Formation of a Catalytic Hydrazone through an Energy Ratchet Mechanism *Angew.Chem.Int.Ed.* **2023**, *62*, e202307530
4. Marchetti, T. (+); Roberts, B.M.W.(+); Frezzato, D.; Prins, L.J. A Minimalistic Covalent Bond-Forming Chemical Reaction Cycle that Consumes Adenosine Diphosphate, **2024**, submitted.