Intrinsically unidirectional chemically fuelled rotary molecular motors

K. Mo, Y. Zhang, Z. Dong, Y. Yang, X. Ma, B. L. Feringa, D. Zhao, *Nature,* **2022***, 609,* 293–298.

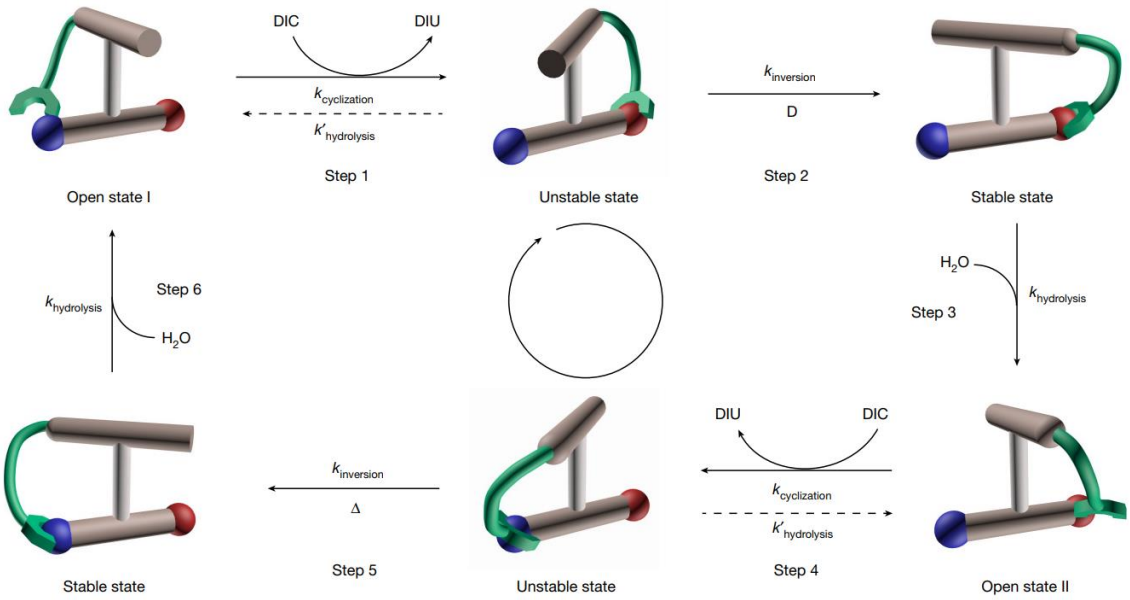

Fig 1: Schematic representation of the continuously clockwise 360° rotary process of the molecular motor fuelled by chemical energy (green, the carboxylic acid group with two chiral centres at the rotor; red and blue, the hydroxyl groups at the stator).

Who are the corresponding authors and what are their research areas?

Ben L. Feringa – *Professor of Chemistry at the University of Gronignen, Netherland*
His research interest is focused on synthetic and physical organic chemistry inspired by nature's principles using the concept of molecular assembly, recognition, transport, motion and catalysis.

Depeng Zhao – *Professor of Pharmaceutical Science at Sun Yat-Sen University, China*
He interested in catalysis asymmetric reactions for the development of medicinal precursors.

What is the main claim of the article?

The authors show the development of an autonomous unidirectional rotary molecular motor (360°) fuelled by chemical energy. They succeed to govern the kinetic bias of the sequential reaction and be able to control selectively the direction of the rotation by taking an advantage of intrinsic chiral elements in the system.

How is it demonstrated?

The evolution of the strategically designed molecular motors is presented to raise an idea of the kinetic biased process or, in another word, the selectivity of the sequential reactions controlled by the adjacent stereocenters. The authors have designed the system to predominantly facilitate kinetic products which are essential to avoid random Brownian motion. (Fig. 2)

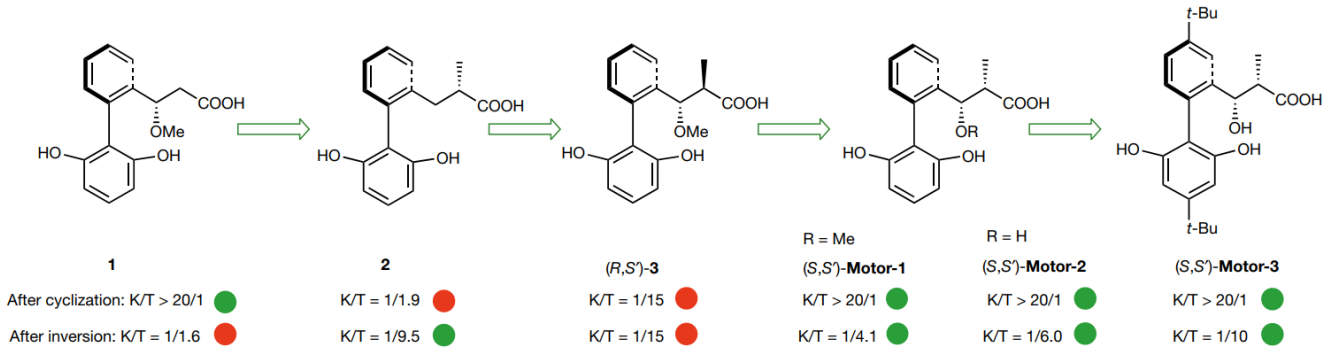

Fig. 2: Evolution of the structures of molecular motors designed and the ratios of kinetic/thermodynamic (K/T) products after cyclization and helix inversion.

To verify the unidirectional 360° rotation of the molecular motor, since the clockwise 360° process consists of six steps, it is necessary to have the distinguishable isomers after each step to allow individual steps studied by 1H NMR. Thus, the motor is desymmetrized in the stator part by introducing one Br-substituent and finally be able to show all distinct isomers during the unidirectional rotary cycle.

The authors also show and present the capability of the optimized molecular motor with the two possessing operation modes: synchronized motion with pulses of a chemical fuel and acid-base oscillations (Fig. 3a); and autonomous motion in the presence of a chemical fuel under slightly basic aqueous conditions (Fig 3b.).

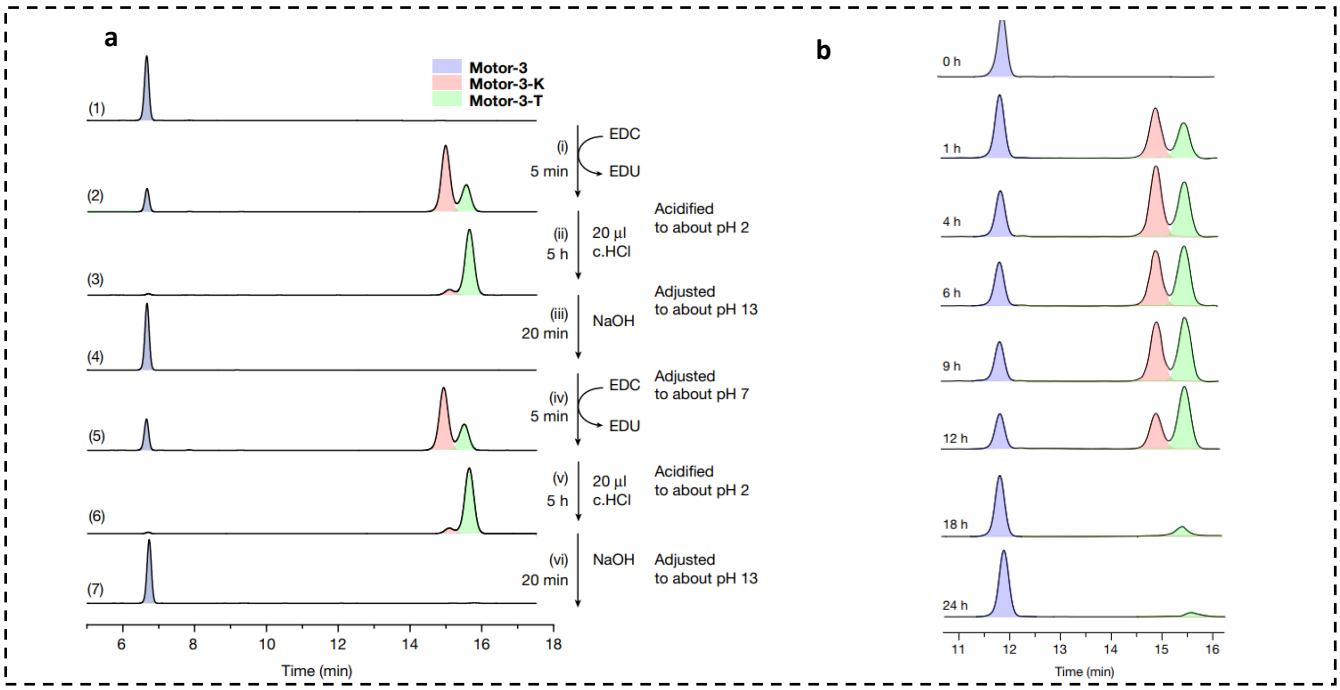

Fig. 3: (a) Synchronized 360° rotation with pulses of chemical fuel and acid– base oscillations. Reagents and conditions: Motor-3 (5 mg, 0.013 mmol), DCM (2.0 ml), H2O (3.0 ml), 25 °C (Supplementary Section 10, Agilent Pursuit XRs 5 C18 250 × 4.6 mm, 25 °C, 1.0 ml min−1, MeCN/H2O/HCOOH = 70/30/0.1, λ = 280 nm). (1) HPLC trace of the initial state of the Motor-3. (2) HPLC trace of the sample taken from the reaction mixture after cyclization for 5 min. (3) HPLC trace of the sample taken from the reaction mixture after inversion. (4) HPLC trace of the sample taken from the reaction mixture after hydrolysis. From (1) to (4), 180° rotation of the molecular motor has been achieved in a unidirectional manner. Then (5), (6) and (7) show the second half of the cycle to achieve full 360° unidirectional rotation. (b) HPLC chromatograms of the samples taken from the reaction mixture during the continuous rotation of the Motor-3 from 0 h to 24 h

Measurement of hydrolysis rate and dynamic kinetic hydrolysis experiment was performed to support and confirm the kinetic bias between kinetic and thermodynamic product to amplify the unidirectionality.

Importantly, the condition that is compatible with both cyclization and hydrolysis was established allowing an efficient continuous rotation of the motors. The rate constant of cyclization and hydrolysis were determined. If some assumptions are accepted, the results indicate that the rate constants meet the proper principles:

1. $k_{cyclization}$ and $k_{hydrolysis}$ should be similar
2. $k_{inversion} > k'_{hydrolysis}$

What are the typical experimental conditions?

- Analytical reversed-phase HPLC (HPLC, Thermo Fisher Dionex Ultimate 3000, Hypersil Gold 250 × 4.8 mm) was used to determine the concentration profile of the products by isocratic elution (MeCN/H_2O/HCOOH=70/30/0.1 v/v/v).
- UV-Vis (Agilent Cary 8454 UV-Vis spectrophotometer) in MeCN solution (~5×10^{-5} M) for the measurement of the energy barrier
- Compatible autonomous condition: Motor-3 (20 mg, 0.05 mmol), 2 M K_3PO_4 aqueous solution (5.0 ml), t-BuOH (3.0 ml), 1,4-dioxane (2.0 ml), DIC (2.0 mmol), HOBt (1.0 mmol), 35 °C

Which are the key related papers?

1. B. S. L. Collins, J. C. M. Kistemaker, E. Otten, B. L. Feringa, *Nat. Chem.* **2016**, *8*, 860 – 866.
2. Y. Zhang, Z. Chang, H. Zhao, S. Crespi, B. L. Feringa, D. Zhao Chem. 2020, 6, 2420 – 2429.
3. S. Borsley, E. Kreidt, D. A. Leigh, B. M. W. Robert *Nature,* **2022**, *604*, 80 – 85.