Title	Emergence of Macroscopic Driving from Light-Powered Conformational Motions

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Project description (2 page max):

Biomolecular machines convert the energy harvested from the environment to produce specific functionality. A prototypical example is the kinesin, namely, a protein transporting cargos along microtubules by hydrolyzing ATP. This has inspired the design and synthesis of artificial molecular machines, capable of producing precise intramolecular motions and with the potential impact for applications ranging from biomedical to smart materials [1]. However, their exploitation for useful functionality relies on the amplification of intramolecular motions to higher length scales, generating a mechanical action on the environment. This can be achieved by, for instance, by anchoring molecular machines to surfaces and polymers, or by incorporating them in structured environments, like gels, supramolecular assemblies, and liquid crystals. In such soft materials, the amplification occurs *via* the dynamical and mechanical coupling between the intramolecular motions and large-scale deformations of the environment.

This project aims to formulate a theoretical understanding of the mechanism underlying the emergence of active motions, at the single molecule level as well as at the macroscopic level. It will focus on systems composed of light-powered rotary motors, which perform continuous unidirectional rotation through sequential photoisomerization and thermal relaxation [2]. To do so, four main objectives will be addressed.

Objective 1. Kinetic Modeling of Conformational Changes.

Simple rotary motors characterized by unidirectional conformational changes when driven out of equilibrium by light will be selected. The aim is to **model the conformational changes in terms of a kinetic process.** The challenge consists of coarse-graining the full dynamics of the motors, which involves light-populated excited states, in terms of transitions between different conformations only, suitable to be used in the subsequent models.

Objective 2. Coupling between Conformational Changes and Roto-Translational Motions.
The motors' dynamics will be examined when they are embedded in an isotropic environment [3]. The coupling between the motors' position and orientation, on the one hand, and the conformations, on the other hand, will be investigated. The aim is to identify the minimal conditions such that **directional global roto-translation, namely, an active motion, can emerge** when only the conformational degrees of freedom are maintained out of equilibrium. The challenge is in accounting for how the energy harvested by the conformational degrees of freedom can be transduced and used by the roto-translational ones to stay out of equilibrium.

Objective 3. Coupling Between Conformational Changes and the Environment.
The motors' dynamics will be examined when they are embedded in a structured environment, such as a lipid bilayer. The first aim is to understand if and how conformational changes can generate **macroscopic changes in the environment.** The second, and more important, aim is to understand if the changes in the environment **result** from either keeping the motor in **nonequilibrium conformations** [4] or from the **dynamical coupling** between the unidirectional motion and the environment. The challenge is in accounting for how the energy harvested by the conformational degrees of freedom can be transduced and used to generate a macroscopic change in the environment.

Objective 4. Thermodynamic Cost.
The processes examined in Objectives 2 and 3 can emerge because part of the energy harvested from light by the conformational degrees of freedom is transduced to maintain either the roto-translational degrees of freedom of the motors or the environment out of equilibrium [5]. In this objective, the aim is to develop a thermodynamic approach to quantify the **efficiency of this transduction.** To do so, all the models developed in the previous Objectives must be thermodynamically consistent: they must account for all mechanisms dissipating energy.

Methods. The project will make use of Quantum Chemical Calculations, Molecular Dynamics Simulations, Stochastic Methods.

[1] Design of collective motions from synthetic molecular switches, rotors, and motors. D. Dattler, G. Fuks, J. Heiser, E. Moulin, A. Perrot, X. Yao, N. Giuseppone. Chem. Rev. 120, 310 (2020).

[2] Designing light-driven rotary molecular motors. D. R. S. Pooler, A. S. Lubbe, S. Crespi, B. L. Feringa, Chem. Sci. 12, 14964 (2021).

[3] Unimolecular submersible nanomachines. Synthesis, actuation, and monitoring. V. Garcia Lopez, P.-T. Chiang, F. Chen, G. Ruan, A. A. Marti, A. B. Kolomeisky, G. Wang, J. M. Tour, Nano Lett. 12, 8229 (2015).

[4] Photoinduced reorganization of motor-doped chiral liquid crystals: bridging molecular isomerization and texture rotation. A. Bosco, M. G. M. Jongejan, R. Eelkema, N. Katsonis, E. Lacaze, A. Ferrarini, B. L. Feringa, J. Am. Chem. Soc. 130, 14615 (2008).

[5] Nonequilibrium thermodynamics of light-induced reactions. E. Pennocchio, R. Rao, M. Esposito, J. Chem. Phys. 155, 114101 (2021).