2023 Tarrach Prize - Les Amis de l'Université

Abstract of the doctoral thesis "Thermodynamics of chemical engines: A chemical reaction network approach" by Dr. Emanuele Penocchio.

I like to describe my thesis as the response to a 2016 *Nature Nanotechnology* editorial article where the journal advocated for a "new generation of physical chemists" able "to connect supramolecular chemistry to the out-of-equilibrium thermodynamic concepts being developed by theoretical physicists", thus providing "a firm grasp of the physical chemistry of out-of-equilibrium systems" [Nat. Nanotechnol. 11, 909 (2016)].

In recent years, experiments in supramolecular chemistry, photochemistry and electrochemistry demonstrated that, by opening synthetic systems to matter and/or energy exchanges with the environment, artificial systems with life-like behaviours can be realized and used to convert energy inputs of different nature into work at both the nanoscopic and the macroscopic level. In analogy to steam engines or electrical engines, such synthetic systems working out-of-equilibrium have been denoted as *chemical engines*. Their relevance for science and technology has been recognized by the 2016 Nobel Prize in Chemistry, awarded to some of the experimental pioneers in the field. On the one hand, chemical engines are building blocks for new active materials engineered at the nanoscale to sense and react as biological structures do. On the other hand, they have been transforming the knowledge of molecular-level dynamic systems. They are advantageous, simplified model systems helping to unveil the working mechanisms of their much more complex biological counterparts found in every cell.

However, it is widely acknowledged that, until now, attempts to synthesize chemical engines have been driven by chemical intuition and serendipity, with little opportunity to reliably judge the effectiveness of a chemical engine's design before it has been realized experimentally. In particular, one tool lacking when I started my PhD was a firm grasp of the thermodynamics of these chemical engines. In my thesis, starting from the state-of-the-art theory of nonequilibrium thermodynamics of chemical reaction networks developed by my PhD supervisor Prof. Massimiliano Esposito at the University of Luxembourg, I extended it to capture essential aspects of out-of-equilibrium supramolecular systems. Among those, I was able to treat rigorously non-ideal [J. Chem. Phys. 154, 094114 (2021)] and light-driven [J. Chem. Phys 155, 114101 (2021)] systems and generalize aspects of information thermodynamics to deterministic chemical reaction networks [J. Chem. Phys. 157, 034110 (2022)], a class of systems that is particularly relevant to study synthetic chemical engines. I also demonstrated that many systems of interest in supramolecular and systems chemistry fall into a particular class of deterministic chemical reaction networks called bipartite networks [J. Chem. Phys. 157, 034110 (2022)]. Furthermore, I introduced original ways to quantify the thermodynamic efficiency of chemical engines [Nat. Commun. 10, 1 (2019), J. Chem. Phys. 157, 034110 (2022)]. Leveraging the theoretical tools I developed, I collaborated with two leading experimental groups in supramolecular chemistry, namely Professor David Leigh's and Professor Alberto Credi's. Thanks to my theoretical modelling, we could use original experimental data to evaluate the thermodynamic efficiency and energy storage capability of a catalysis-driven molecular motor [Nat. Chem. 14 (5), 530-537 (2022)] and a light-driven self-assembling molecular pump [Nat. Nanotechnol. 17, 746 (2022)]. The editorial board of *Nature Nanotechnology* highlighted the latter contribution through a

dedicated article in their News and Views series [Nat. Nanotechnol. **17**, 675 (2022)]. Such a new theoretical understanding led to proposing novel thermodynamics-based design principles and optimization strategies for molecular motors and related systems [J. Am. Chem. Soc. 144 (44), 20153-20164 (2023), Small, 2206188 (2023)].

Overall, my thesis builds a general thermodynamic level of understanding of chemical engines, complements previous analyses based on kinetics and stochastic thermodynamics, and has practical implications for designing and improving synthetic systems, regardless of the particular type of powering or chemical structure. It also provided a meaningful, practical outcome that connects supramolecular chemistry to out-of-equilibrium thermodynamics and illustrates the significance and impact that can arise from making such connections. In the words of the external thesis committee member Prof. Thomas Hermans, a world-class experimenter in supramolecular chemistry recently awarded an ERC consolidator grant in the area, the outputs of my doctoral research "will become reference works in the field of molecular motors" and offer "new insights into the concept of 'power stroke' in molecular machines, which has been fiercely debated in the recent years (between Nobel Laureate Martin Karplus and renowned physicist Dean Astumian). This is incredibly exciting". The other external thesis committee member, Prof. David Sivak, a leading theoretician in information thermodynamics, recognized that "this is the most impactful doctoral thesis I have examined or overseen as a thesis-committee member". The whole thesis committee "was impressed by comprehensiveness and interdisciplinarity of the thesis as well as by the scientific output".

Because of the above results, I was awarded the 2022 Foresight Institute Distinguished Student Award, an international prize recognizing the PhD student "whose work is considered most notable in advancing the development and understanding of nanotechnology". Also, with my PhD supervisor Prof. Massimiliano Esposito and our collaborators from the Leigh Group, we received the 2023 Royal Society of Chemistry Horizon Prize for Physical Organic Chemistry, a shared international prize "for breakthroughs in catalyzed nonequilibrium systems, particularly molecular ratchet mechanisms, that have provided fundamental insights into the dynamics of matter"[1].

My results have been presented at several international conferences in physics and chemistry (including two March Meetings of the American Physical Society, the 2021 Systems Chemistry Virtual Symposium, and the 2022 Systems Chemistry Gordon Research Conference). I have also been invited to give seminars about my thesis at the University of Oxford, the Supramolecular Science and Engineering Institute in Strasbourg and the Pennsylvania State University. The number and interdisciplinarity of my dissemination activities reiterate the contribution of my thesis to the generation and communication of new ideas, tools, and knowledge, as well as its broad impact on several research communities, from theoretical physics to synthetic chemistry.

1 This information is embargoed until 13 June 2023. Please, treat is confidentially.