Proceedings of CONF-APMM 2025 Symposium: Multi-Qubit Quantum Communication for Image Transmission over Error Prone Channels
DOI: 10.54254/2753-8818/2025.GL24596

Thermodynamic Perspectives on Molecular Motors: Energy Conversion, Efficiency, and Non-equilibrium Dynamics

Quanrui Chen

University of Washington, Washington, USA
chenquanrui040605@163.com

Abstract. Molecular motors are sophisticated protein complexes that transform chemical energy into directed mechanical motion, underpinning critical cellular processes such as intracellular transport, cell division, and muscle contraction. Operating far from equilibrium, these motors challenge classical thermodynamic descriptions, necessitating frameworks like stochastic thermodynamics and fluctuation theorems to describe their energy conversion, efficiency, and entropy production quantitatively. This review synthesizes theoretical understandings of molecular motor operation, highlighting the integration of stochastic thermodynamics with computational simulations and cutting-edge experimental techniques, including nanopore-based single-molecule measurements. Key topics discussed include mechanisms of motion, thermodynamic efficiency, performance trade-offs, and the essential role of entropy production in maintaining directionality. Finally, we identify unresolved challenges and suggest future research directions to deepen our fundamental insights and enhance practical applications in biotechnology and nanotechnology.

Keywords: Molecular motors, stochastic thermodynamics, entropy production, thermodynamic efficiency

1. Introduction

Molecular motors are protein complexes capable of converting diverse energy sources into mechanical motion. They underpin virtually all vital life processes—including intracellular transport, signal transduction, cell division, and muscle contraction.Intriguingly, these motors exhibit efficient functionality within highly viscous, low Reynolds number milieus, typified by overdamped dynamics and substantial thermal fluctuations [1]. Beyond their biological functions essential to cellular viability, molecular motors also inspire the design of artificial nanomachines in fields such as chemistry and nanotechnology.

Molecular motors function under non-equilibrium thermodynamic conditions, continuously converting chemical energy into directed motion while experiencing persistent thermal fluctuations. Such conditions challenge the descriptive power of classical equilibrium thermodynamics.Stochastic thermodynamics extends classical thermodynamic principles—including heat, work, and entropy—to individual molecular trajectories, thereby furnishing a rigorous quantitative framework for the analysis of microscopic systems [2]. Central to this approach are fluctuation theorems, which quantitatively link the probabilities of forward and reverse molecular trajectories, elucidating

© 2026 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2025.GL24596

irreversibility and entropy production. Astumian [3] elucidated the efficacy of modeling molecular motors, such as kinesin and myosin V, as stochastic chemical systems, wherein thermally driven transitions between states are observed. This perspective has significantly enhanced our understanding of how directed motion emerges at the molecular scale despite intrinsic noise and randomness. Thus, stochastic thermodynamics provides a rigorous foundation for evaluating molecular machines' efficiency, performance, and directionality by analyzing the intricate interplay among chemical reactions, mechanical work, and entropy production.

This review examines molecular motors from thermodynamic and nonequilibrium dynamic perspectives. Initially, the biological significance will be explored, followed by a discussion of theoretical frameworks—encompassing stochastic thermodynamics and fluctuation theorems—to elucidate energy conversion mechanisms, efficiency constraints, and operational dynamics. Finally, it highlight current challenges and open questions driving future research.

2. Classification and mechanisms of molecular motors

Molecular motors are specialized proteins that convert chemical energy into mechanical work, facilitating directed movement and molecular transformations within cells. The aforementioned processes are inherently cyclic, governed by the principles of nonequilibrium thermodynamics. Specifically, the hydrolysis of ATP or the incorporation of nucleotides instigates conformational alterations, which subsequently manifest as discrete mechanical displacements. Understanding their mechanisms requires examining how specific biochemical reactions trigger structural shifts that, in turn, lead to motion.

Kinesin is a microtubule-associated motor protein that uses ATP to drive processive movement toward the microtubule's plus end. In one cycle, ATP binds to the leading motor head attached to the microtubule. This binding triggers a conformational change—neck linker docking—that pulls the rear head forward. The new leading head releases ADP and binds to the following tubulin site. In contrast, the trailing head hydrolyzes ATP and releases inorganic phosphate (Pi), detaching and preparing for the next step. This coordinated sequence results in continuous forward stepping, converting chemical free energy into mechanical displacement.

Conversely, dynein translocates toward the microtubule's minus end, exhibiting a more intricate architecture characterized by a ring of AAA+ ATPase domains and an extended coiled-coil stalk. ATP binding at the AAA1 site initiates a dramatic conformational rearrangement in the linker domain, generating a power stroke that shifts the cargo-bound tail forward. Following ATP hydrolysis and phosphate release, dynein's microtubule-binding domain changes affinity, enabling detachment, stepping, and rebinding. The coordination of hydrolysis across AAA domains governs dynein's irregular but processive stepping behavior.

Myosin V functions on actin filaments through a comparable chemomechanical mechanism. The binding of ATP to the lagging head induces its dissociation from actin. Hydrolysis to ADP and Pi primes the head for the next step. While the leading head remains attached, the trailing head swings forward in a lever-arm motion and binds further along the filament. Release of Pi and ADP completes the cycle. Directional bias arises from strain-induced gating between the heads, promoting forward steps.

Helicases unwind nucleic acids by translocating along one strand and destabilizing the duplex. ATP binding and hydrolysis induce conformational changes that propel the enzyme forward. Energy released traps transient base-pair openings (passive mechanism) or actively destabilises base pairs (active mechanism), enabling translocation and strand separation.

DOI: 10.54254/2753-8818/2025.GL24596

Polymerases synthesize DNA or RNA by adding nucleotides to a growing strand. Each incorporation begins with binding of a complementary dNTP to the active site. Upon correct base pairing, a conformational change positions the nucleotide for catalysis. The 3′-OH of the primer attacks the α-phosphate of the dNTP, forming a phosphodiester bond and releasing pyrophosphate (PPi). This energetically favorable reaction drives the polymerase to the next templating base, tightly coupling chemical events to directional movement.

Molecular motors function far from equilibrium, perpetually transforming free energy into directed motion amidst thermal fluctuations. Stochastic thermodynamics provides a framework for elucidating the integration of discrete chemical transitions, free energy landscapes, and conformational dynamics into stable, directional cycles of molecular work.

3. Non-equilibrium thermodynamics of molecular motors

3.1. Energy conversion under nonequilibrium conditions

Molecular motors operate fundamentally as nonequilibrium systems, driven by continuous chemical energy input, typically from ATP hydrolysis or nucleotide incorporation. Unlike equilibrium processes, these systems maintain directional motion and sustain mechanical work despite persistent thermal fluctuations. Molecular motors' ability to convert chemical free energy into mechanical displacement differentiates them from equilibrium systems, situating them within stochastic thermodynamics and nonequilibrium physics.

Such transduction processes occur under conditions far from equilibrium, where classical thermodynamics no longer comprehensively describes system behavior.

Stochastic thermodynamics provides a rigorous framework that generalizes classical thermodynamic concepts—such as heat, work, and entropy production—to individual molecular trajectories of systems out of equilibrium.This theory delineates thermodynamic quantities along fluctuating trajectories, facilitating the quantitative analysis of microscopic nonequilibrium processes in molecular motors. In particular, molecular motors exemplify systems governed by Markovian dynamics, either described by continuous Langevin equations or discrete-state master equations, both of which satisfy local detailed balance and thus ensure thermodynamic consistency at microscopic scales [4].

Central to this framework are fluctuation theorems, which quantitatively connect the probability distributions of forward and reverse molecular trajectories, effectively quantifying irreversibility. These theorems establish essential limitations on the probabilities of energy conversion processes and the corresponding entropy generation. Such constraints clarify how chemical energy input, such as ATP hydrolysis, biases transitions between states to produce directed motion and mechanical work output, despite the inherent stochasticity of thermal fluctuations[2,5].

In summary, molecular motors achieve directed mechanical motion by continuously consuming chemical-free energy and converting it into work while operating far from equilibrium. The interplay between chemical reactions, mechanical displacement, and entropy production within the stochastic thermodynamic framework provides a powerful conceptual basis for analyzing molecular motor operation's energetic and thermodynamic characteristics.

3.2. Stochastic thermodynamics and fluctuation theorems

Classical thermodynamics falls short at describing molecular motors due to the prominence of thermal fluctuations at microscopic scales. Stochastic thermodynamics extends classical concepts—

DOI: 10.54254/2753-8818/2025.GL24596

such as heat, work, and entropy—to the level of individual stochastic trajectories, providing a robust theoretical framework to analyze nonequilibrium molecular systems. This framework guarantees thermodynamic consistency by imposing a local detailed balance condition on the transition rates between states or the corresponding noise correlations in continuous Langevin dynamics. This ensures that the probabilities of state transitions are directly connected to thermodynamic forces, such as chemical potential gradients or mechanical loads[2].

Central to stochastic thermodynamics are fluctuation theorems, which rigorously quantify the irreversibility of nonequilibrium processes by relating the probabilities of forward and reverse trajectories. The Crooks fluctuation theorem links the probability distributions of work in forward and reverse processes, generalizing classical second-law inequalities into equalities for fluctuating quantities. Similarly, the Jarzynski equality provides a powerful method to relate nonequilibrium work to equilibrium free-energy differences. These theorems underscore the fundamental relationship between fluctuations, dissipation, and irreversibility, offering precise constraints on energy conversion and entropy production within molecular motors[2].

Molecular motors such as kinesin and myosin V illustrate these principles vividly. Their dynamics can be viewed as stochastic random walks on a network of chemical states.Each state reflects a distinct biochemical configuration, with transitions driven by ATP binding, hydrolysis, or product release. The principle of microscopic reversibility in chemical reactions indicates that the probabilities of forward and reverse transitions are underpinned by thermodynamic conditions, particularly the chemical potential differentials of ATP, ADP, and inorganic phosphate (Pi). The directional bias of motor motion thus emerges naturally from chemically induced asymmetries in transition probabilities rather than from mechanical constraints alone [3].

Overall, stochastic thermodynamics and fluctuation theorems provide profound insights into the thermodynamic behavior of molecular motors. They demonstrate that the efficiency and directionality of molecular motors are intimately tied to their underlying stochastic dynamics and chemical kinetics. Such insights deepen our fundamental understanding of biological machines and guide the design of synthetic molecular motors and nano-devices operating far from equilibrium.

3.3. Efficiency and performance trade-offs

The thermodynamic efficiency of a molecular motor is classically defined as the ratio of sound work output to the chemical free energy input per cycle. For motors powered by ATP hydrolysis, this corresponds to the fraction of the free energy drop $\Delta\mu$ (from ATP to ADP + Pi) successfully converted into mechanical work. Thermodynamic efficiency can theoretically approach unity under ideal conditions in tightly coupled motors such as F1-ATPase, where each hydrolysis event leads to one mechanical step [6]. However, practical operation is constrained by thermal fluctuations and kinetic bottlenecks.

A key concept in assessing motor performance is the stall force, the external load at which forward motion ceases and net work output drops to zero. While efficiency reaches its maximum at stall, power output vanishes. Conversely, motors often operate at a significantly reduced efficiency at maximum power. This reflects a fundamental power-efficiency trade-off, where high output power comes at the cost of increased dissipation and reduced efficiency [7].

Recent developments in stochastic thermodynamics have formalized this trade-off. In particular, the thermodynamic uncertainty relation (TUR) establishes that the entropy production rate is constrained by the relative precision of an output observable, such as the displacement of a motor or the number of ATP molecules hydrolysed. Specifically, a minor variance in output (higher precision)

DOI: 10.54254/2753-8818/2025.GL24596

demands higher dissipation. This implies that motors achieving high precision and power must incur greater energetic costs [8].

Pietzonka and Seifert [7] derived a universal bound incorporating power fluctuations, demonstrating that steady-state heat engines—including biomolecular motors—must balance three competing factors: mean power output, efficiency, and constancy. Their inequality reveals that approaching Carnot efficiency at finite power output is only feasible if power fluctuations become significantly large, an impractical condition in realistic molecular machines. The formal bound is given by:

$$\frac{P(\eta_C-\eta)}{\eta T_c \Delta P} \leq \frac{1}{2} \tag{1}$$

Where P is the mean output power, η_C is the Carnot efficiency, η is the actual efficiency, T_c the cold reservoir temperature, and ΔP the power fluctuation [7]. This highlights that constancy—i.e., low fluctuations—is equally crucial for nanoscale engines as high power output and efficiency.

Together, these results illustrate that the functional optimization of molecular motors is not solely about maximizing efficiency or speed but involves strategic trade-offs between efficiency, power, stability, and precision. The thermodynamic uncertainty framework provides a unifying perspective to quantify and interpret these trade-offs across biological and synthetic motors operating under nonequilibrium conditions.

3.4. Entropy production and directionality

Entropy production is fundamental to the operation of molecular motors, underpinning their ability to perform directed mechanical tasks in noisy thermal environments. At the microscopic level, sustained directional motion necessitates ongoing entropy production, underscoring the intrinsic irreversibility of the chemical cycles propelling these motors. According to stochastic thermodynamics, entropy production quantifies the irreversibility associated with energy dissipation, and it arises naturally whenever a system is driven out of equilibrium through processes like ATP hydrolysis or nucleotide incorporation [2].

Directional stepping in molecular motors, such as kinesin and myosin, can be viewed as a statistical consequence of biased state transitions induced by differences in chemical potentials. Each motor step corresponds to a dissipative event, characterized by a positive entropy production. Thus, maintaining directionality and reliable mechanical output necessitates constant energy dissipation, linking thermodynamic irreversibility directly to functional performance. [3] Explicitly highlights that molecular motors exploit entropy production to maintain directional bias, effectively converting chemical free energy into directional movement. Without continual entropy production, the motor's movement would cease to exhibit a directional bias, effectively losing its functional utility in biological systems.

Therefore, entropy production is an unavoidable inefficiency and a critical thermodynamic requirement enabling robust directional motion at the nanoscale.

4. Computational and experimental studies

Both computational simulations and experimental methodologies have significantly driven advances in our understanding of molecular motors. Computational methods, particularly Langevin and molecular dynamics (MD) simulations, have revealed microscopic details of motor operations, energetics, and efficiency. Software packages such as LAMMPS facilitate detailed modeling of

DOI: 10.54254/2753-8818/2025.GL24596

molecular motors, capturing dynamic trajectories and providing insights into mechanochemical coupling and thermodynamic performance at nanoscale resolution.

Experimentally, techniques such as optical tweezers and single-molecule fluorescence microscopy have directly measured mechanical properties and motion trajectories of molecular motors like kinesin, dynein, and myosin. Single-molecule force spectroscopy further complements these methods by quantifying the forces and mechanical steps associated with individual ATP hydrolysis events, providing precise data on energy conversion efficiency and power output [8].

A compelling recent advancement is single-molecule picometer-resolution nanopore tweezers (SPRNT), which employ modulation of ionic currents through a nanopore to monitor molecular motors at sub-angstrom spatial resolution and millisecond temporal resolution [9]. This methodology has been efficaciously implemented in the study of helicases, exemplified by Hel308, wherein discrete kinetic substates have been delineated within the ATP hydrolysis cycles. Such precise measurements validate theoretical models derived from stochastic thermodynamics, explicitly linking microscopic chemical transitions to macroscopic mechanical outputs.

Computational and experimental approaches complement each other effectively: computational methods offer theoretical predictions and microscopic insights, while experimental methods provide direct measurements and validate motor behaviors under physiological conditions. Integrating these approaches, particularly through nanopore-based techniques, substantially enhances our understanding of the thermodynamic principles governing molecular motors, highlighting the importance of sequence-dependent dynamics in motor functionality and regulation.

5. Conclusion

Integrating stochastic thermodynamics, fluctuation theorems, and advanced single-molecule experimental techniques has significantly deepened our understanding of molecular motors. Despite these advancements, several important questions remain unresolved. Future research should elucidate atomic-scale energy transduction mechanisms, refine theoretical frameworks, and explore efficiency and power limits under biological constraints.

Experimental methods such as nanopore tweezers (SPRNT) and computational simulations will likely play central roles in addressing these challenges. Enhanced spatiotemporal resolution in single-molecule studies promises unprecedented elucidation of sub-step kinetics and transient intermediates, bridging theoretical and empirical divides. Advanced computational techniques, leveraging robust hardware and refined algorithms, will enable comprehensive analyses of motor dynamics and efficiency landscapes, overcoming current constraints.

In conclusion, molecular motors represent an ideal platform to explore fundamental principles of nonequilibrium thermodynamics, efficiency trade-offs, and entropy production at microscopic scales. Continued integration of theoretical, computational, and experimental approaches promises deeper fundamental insights and practical applications in nanotechnology, medicine, and biotechnology.

References

[1] Iino, R., Kinbara, K., & Bryant, Z. (2020). Introduction: Molecular Motors. Chemical Reviews, 120(1), 1–4. https: //doi.org/10.1021/acs.chemrev.9b00819

[2] Seifert, U. (2012). Stochastic thermodynamics, fluctuation theorems and molecular machines. Reports on Progress in Physics, 75(12), 126001. https: //doi.org/10.1088/0034-4885/75/12/126001

[3] Astumian, R. D. (2010). Thermodynamics and Kinetics of Molecular Motors. Biophysical Journal, 98(11), 2401–2409. https: //doi.org/10.1016/j.bpj.2010.02.040

DOI: 10.54254/2753-8818/2025.GL24596

[4] Gennerich, A., & Vale, R. D. (2009). Walking the walk: how kinesin and dynein coordinate their steps. Current Opinion in Cell Biology, 21(1), 59–67. https: //doi.org/10.1016/j.ceb.2008.12.002
[5] Brown, A. I., & Sivak, D. A. (2020). Theory of Nonequilibrium Free Energy Transduction by Molecular Machines. Chemical Reviews, 120(1), 434–459.
[6] Li, C.-B., & Toyabe, S. (2020). Efficiencies of molecular motors: a comprehensible overview. Biophysical Reviews, 12(2), 419–423. https: //doi.org/10.1007/s12551-020-00672-x
[7] Pietzonka, P., & Seifert, U. (2018). Universal Trade-Off between Power, Efficiency, and Constancy in Steady-State Heat Engines. Physical Review Letters, 120(19). https: //doi.org/10.1103/physrevlett.120.190602
[8] Bustamante, C., Cheng, W., & Mejia, Y. X. (2011). Revisiting the Central Dogma One Molecule at a Time. Cell, 144(4), 480–497. https: //doi.org/10.1016/j.cell.2011.01.033
[9] Derrington, I. M., et al. (2015). Subangstrom single-molecule measurements of motor proteins using a nanopore. Nature Biotechnology, 33(10), 1073–1075. https: //doi.org/10.1038/nbt.3357