Molecular Motor or Molecular Clock: A Question of Load

Henry Hess

Abstract—The output of a motor is work, while the output of a clock is information. Here it is discussed how a molecular motor can produce both, work and information, depending on the load. If the ratio of the backward and forward stepping rates of a molecular motor increases exponentially with load, the change in free energy per step can be used to produce only work (at stall force) or only timing information (at zero force), or anything in between.

Index Terms—Molecular motor, second law of thermodynamics, clock.

It could be argued that in the absence of a load, a running motor pointlessly wastes the input energy. However, if the motor runs at a constant speed it can be used as a clock—a machine providing us with information about the passage of time. In the past, clocks were macroscopic entities consuming many kB T per tick, but circadian clocks [1] and radical clocks [2] demonstrate that timing information can also be generated at the molecular scale. Here, the focus is on the timing information generated by the stepping of a molecular motor, which utilizes an energy input to advance against an external load. An example of such a molecular motor is a kinesin motor protein, which autonomously hydrolyzes ATP and takes 8 nm steps along a microtubule while pulling external loads of up to 7 pN [3]. However, the molecular motor could be driven by other types of energy (e.g. light [4]) and could have an output which is not mechanical work (e.g. charge transport against an electric field) as long as it operates autonomously [5].

How much timing information does a molecular motor produce? If we disregard the stochastic fluctuations in the duration of each step for the moment, and assume that the motor steps at equal time intervals, a molecular motor step produces the same amount of information as the tick of a watch. For a given observation window (e.g. a day), events can be assigned time stamps defining after which time intervals, a molecular motor step produces the same amount of information (e.g. charge transport against an electric field) as long as it operates autonomously [5].

To illustrate this, imagine looking at a molecular clock, which in average takes 1024 forward steps every day. This can be used to divide the day into 1024 time intervals, delivering a 10-bit time stamp every time the clock is examined. However, if in average a backward step may occur, a time stamp such as “500” may indicate 500 forward steps or 501 forward steps and 1 backward step. This reduces the number of distinguishable intervals by half. Meeting a friend at “500 steps” thus indicates a time interval which increases with the rate of backward steps.

Of course, the opposing force also reduces the number of forward steps N in a given time interval unless the motor mechanism is a pure power stroke [7]. However, provided the mechanical and chemical cycles of the motor are tightly coupled and futile cycles are absent, the number of catalytic cycles decreases in proportion to the number of forward steps and the number of significant bits of each time stamp is still given by log2(k+/k−). The conditions of tight coupling and absence of futile cycles may not fully apply in practice depending on the motor and the force-accelerated unbinding of the motor from the filament is not explored here [6], [8], [9], since I aim to describe the most basic case.

The ratio of forward and backward rates allows us to relate average information generated per step C = log2(N/n) to the free energy per step:

$$\Delta G = W - Ck_B T \ln 2$$

(1)

This implies that the molecular motor converts the free energy either into timing information or work. Thus even an unloaded motor (F = 0 and W = 0) delivers something in return for the expenditure of free energy, just as the moving arms of a Swiss watch make the winding worthwhile.

It can be argued that Eq. (1) is merely a restatement of the relationship between free energy, work and forward and backward rates used above in its derivation:

$$\Delta G = W + k_B T \ln (k+/k−)$$

(2)

While the equations are certainly formally equivalent, the point of the analysis is that Eq. (1) describes the operation of a device having aspects of a motor and a clock, while Eq. (2) makes a statement purely about a motor. The physics of a system consisting of an opening and sand under the influence of gravity can be described by mechanics,
but it is still worthwhile to point out that this system can be employed as a sand clock.

The chemical conversion of the ATP and water into ADP and phosphate could of course also be detected by other analytical techniques, such as NMR, instead of measuring the location of a molecular motor by optical microscopy. This would also provide timing information, but remove the possibility of extracting work. Over time, the changing concentrations of the reactants would make the "chemical clock" move slower but also reduce the expenditure of free energy. Just as information can be stored in the concentrations of various small molecules [10], any chemical reaction can serve in principle as a clock. However, autocatalytic reactions displaying an initially accelerating reaction rate are an implementation of Moore’s Clock described by Eliazar and Shlesinger [11].

Looking at a molecular motor as a clock with a load-dependent accuracy is of course closely related to the extensive and insightful recent work of Barato, Pietzonka and Seifert [12]–[16] which explores the relationship between energy dissipation, efficiencies, and precision of molecular machines. Nevertheless, there are some differences in the present approach. In “Cost and Precision of Brownian Clocks” Barato and Seifert [14] aim to determine the energetic cost to measure a given time interval (e.g. an hour) with a given uncertainty and find that the energetic cost is independent of the unit of clock time (the time per tick), that is a clock measuring an hour with a one minute precision by counting seconds requires just as much energy dissipation as a clock counting minutes. This task however resembles the task of an alarm clock (or a fuse) rather than the task of a wrist watch or wall clock. A wrist watch returns timing information continuously, and adding the capability of measuring seconds with a third arm provides additional information to the wearer, which is of interest here. Secondly, Barato and Seifert account for the randomness in the individual transitions, which additionally degrades the timing information. Here, the perspective of a “long-term” average is taken where the noise introduced by the variability in the timing of each step has vanished. This is of course a serious shortcoming if we time a single event occurring after a small number of steps (alarm clock or fuse). However, for a clock continuously producing timing information over a large number of steps, these fluctuations do average out and a simple connection to the thermodynamic quantities defined for equilibrium states can be made.

This long-term, asymptotic perspective is of course a bit anachronistic when discussing a clock, whose specific task is to label events occurring in finite time. In other words, one could argue that a stepping motor is by definition a non-equilibrium system. However, as Astumian discussed in detail [17], the molecular motor is in local thermal equilibrium, and the directionality of the process arises from the asymmetry in the binding rates of the reactants and products produced by their concentrations. Konopik et al. [18] recently presented an analysis of the fundamental energy cost of finite-time computing which estimates energy costs beyond the Landauer limit arising from equilibrium thermodynamics [19]. They concluded that the energetic cost of a finite-time, logically irreversible bit operation is given by the sum of the Landauer limit (kT ln2) and a dissipation term inversely proportional to the process time with a system-specific proportionality constant termed energy efficiency constant. Without exploring the interesting differences in using a molecular motor for computation [20] or as a clock, one can follow this argument and include a dissipative work term in equation (1):

$$\Delta G = W - a_{\text{clock}}/\tau - C_k T \ln 2$$  (3)

where $\tau$ is the time available to complete the step and $a_{\text{clock}}$ is the energy efficiency constant of the clock. The clock energy efficiency constant can be estimated for the example of a kinesin motor with a size of a few nanometers moving in 8 nm steps at a maximum speed of 1 $\mu$m/s in a fluid with a viscosity on the order of 1 mPas as 0.000001 kgTs. Thus, for an individual kinesin motor, the nonequilibrium contribution to the energy consumption is vanishingly small relative to the work or information output.

Other connections can be made to the work of Jarzynski and colleagues, who illustrated how information can be converted into work by a mechanical demon [21], and of course to Landauer’s seminal insight that information erasure requires a minimum of energy dissipation and the developments resulting from it [19]. It should be noted that information in statistical thermodynamics quantifies uncertainty (with larger uncertainty corresponding to a higher information content), whereas “timing information” as used here reduces uncertainty. Therefore, the apparent paradox that both the production of timing information and the erasure of (thermodynamic) information require energy expenditure.

The main message of this discussion is that even an unloaded molecular motor provides a return for an investment in free energy: It can serve as a clock.

References

[1] J. C. Dunlap, “Molecular bases for circadian clocks,” Cell, vol. 96, no. 2, pp. 271–290, Jan. 1999.

[2] I. Kretzschmar, J. A. Levinson, and C. M. Friend, “Hydroxymethylcytosine in biomolecular processes,” Proc. Natl. Acad. Sci. USA, vol. 75, no. 12, Dec. 2012, p. 1223, art. no. E202004227.

[3] J. Howard, “Mechanics of Motor Proteins and the Cytoskeleton,” Sunderland, MA, USA: Sinauer, 2001, p. 367.

[4] J. M. Parrondo, J. M. Horowitz, and T. Sagawa, “Thermodynamics of non-equilibrium processes,” J. Stat. Mechanics: Theory and Exp., vol. 2020, no. 12, 2020, Art. no. 126001.

[5] P. Pietzonka, A. C. Barato, and U. Seifert, “Universal bound on the energetic cost of finite-time computing,” 2021, arXiv:2101.07075.

[6] A. C. Barato and U. Seifert, “Thermodynamic uncertainty relation for biomolecular processes,” Phys. Rev. Lett., vol. 114, no. 15, Apr. 2015, Art. no. 158101.

[7] I. Eliazar and M. F. Shlesinger, “Moore’s clock,” Phys. A, Stat. Mech. Appl., vol. 541, Jun. 2020, Art. no. 123619.

[8] U. Seifert, “Stochastic thermodynamics, fluctuation theorems and molecular machines,” Rep. Prog. Phys., vol. 75, no. 12, Dec. 2012, Art. no. 126001.

[9] A. R. Astumian, “Making molecules into motors,” Scientific Amer., vol. 285, no. 1, pp. 56–64, Jul. 2001.

[10] M. O. Hancock, “The Kinesin-1 chemomechanical cycle: Stepping toward a consensus,” Biophys. J., vol. 110, no. 6, pp. 1216–1225, Mar. 2016.

[11] S. Konopik et al., “Principles of information storage in small-molecule mixtures,” IEEE Trans. Nanobiosci., vol. 19, no. 3, pp. 378–384, Jul. 2020.

[12] I. Eliazar and M. F. Shlesinger, “Moore’s clock,” Phys. A, Stat. Mech. Appl., vol. 541, Jun. 2020, Art. no. 123619.

[13] U. Seifert, “Stochastic thermodynamics, fluctuation theorems and molecular machines,” Rep. Prog. Phys., vol. 75, no. 12, Dec. 2012, Art. no. 126001.

[14] A. C. Barato and U. Seifert, “Thermodynamic uncertainty relation for biomolecular processes,” Phys. Rev. Lett., vol. 114, no. 15, Apr. 2015, Art. no. 158101.

[15] A. C. Barato and U. Seifert, “Cost and precision of Brownian clocks,” Phys. Rev. X, vol. 6, no. 4, Dec. 2016, Art. no. 041053.

[16] P. Pietzonka, A. C. Barato, and U. Seifert, “Universal bound on the efficiency of molecular motors,” J. Stat. Mechanics: Theory Exp., vol. 2016, no. 12, 2016, Art. no. 124004.

[17] P. Pietzonka and U. Seifert, “Universal trade-off between power, efficiency, and constancy in steady-state heat engines,” Phys. Rev. Lett., vol. 119, no. 3, 2018, Art. no. 030602.

[18] R. D. Astumian, “Microscopic reversibility as the organizing principle of molecular machines,” Nature Nano, vol. 7, no. 11, pp. 684–688, 2012.

[19] K. Konopik, T. Korten, E. Lutz, and H. Linke, “Fundamental energy cost of finite-time computing,” 2021, arXiv:2101.07075.

[20] J. M. Parrondo, J. M. Horowitz, and T. Sagawa, “Thermodynamics of information,” Nature Phys., vol. 11, no. 2, pp. 131–139, 2015.

[21] V. Nicolau et al., “Parallel computation with molecular-motor-propelled agents in nanofabricated networks,” Proc. Natl. Acad. Sci. USA, vol. 113, no. 10, pp. 2591–2596, Mar. 2016.

[22] Z. Lu, D. Mandal, and C. Jarzynski, “Engineering Maxwell’s demon,” Phys. Today, vol. 67, no. 8, p. 60, 2014.