Supporting Information for “Sterically Driven Current Reversal in a Molecular Motor Model”

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I. DRIVING FORCE

The concentration of FTC, ETC, and C was controlled by setting the external chemical potentials \( \mu'_{\text{FTC}} \), \( \mu'_{\text{ETC}} \), and \( \mu'_{C} \), respectively (detailed in SI Sec. VI). As \( l_1 \) was varied, the simulation cell was contracted or expanded along the perpendicular dimensions so the simulation volume remained fixed. By maintaining a high concentration of FTC and low concentrations of ETC and C, we placed the motor in a nonequilibrium steady state. Unless specified otherwise, all simulations in this study used \( \mu'_{\text{FTC}} = 0 \) and \( \mu'_{\text{ETC}} = \mu'_{C} = -10.0 \), which maintained an average of 8.7 FTC molecules, 0.2 ETC molecules, and 1.4 C particles in the simulation volume. In Fig. S1a we show the motor’s current as a function of \( l_1 \) spacing for several FTC concentrations, spanning both near-to and far-from-equilibrium regimes. When there is no FTC present the motor is in equilibrium and produces no appreciable current. Increasing the number of FTC generates more current—negative current at low \( l_1 \) and positive current at high \( l_1 \). While the FTC concentration controls the magnitude of the current, it has no effect on the motor’s direction. After catalytic sites become saturated additional fuel molecules have no effect on the motor’s performance, resulting in a plateau in plots of current versus the average number of FTC molecules, \( \langle N_{\text{FTC}} \rangle \).

![Graph showing current as a function of FTC concentration](image)

**FIG. S1.** FTC concentration affects motor current magnitude, but not direction. (a) Current as a function of \( l_1 \) spacing in the linear motor for \( l_2 = 0 \) is shown for several values of average number of FTC molecules \( \langle N_{\text{FTC}} \rangle \) in the fixed simulation volume. (b) Current as a function of \( \langle N_{\text{FTC}} \rangle \) for \( l_1 = 1 \) (red) and \( l_1 = 12 \) (black). Data points and error bars at \( l_1 = 0 \) and \( \langle N_{\text{FTC}} \rangle \approx 0.0, 0.5, 3.3 \) represent mean and standard error across 200 independent simulations. All other data points and error bars are given by the mean and standard error across 100 independent simulations. All simulations have \( 2 \times 10^8 \) time steps of size \( \Delta t = 5 \times 10^{-3} \).

II. PERIODIC BOUNDARY CORRELATIONS

We presented two closely related geometries for motors, the catenane rings and the linear motor with periodic boundary conditions. That linear motor had only three motifs regardless of the spacings \( l_1 \) and \( l_2 \). Due to the periodic boundary conditions, the linear motor’s shuttling ring effectively saw more motifs, but the states of those periodic replica motifs were correlated. One might worry that those correlations would make it problematic to compare, for example, a six-motif ring motor with a three-motif linear motor. Even if the two geometries had identical spacings, the period boundary condition correlations would differ. We confirmed that these correlations did not appreciably affect the results or analyses, as shown in Fig. S2. By increasing the number of explicit motifs in the linear motor from...
three to nine, and therefore decreasing correlations, the current is not significantly affected and the current reversal is unchanged.

FIG. S2. Current reversal persists as the number of motifs \( N_{\text{motif}} \) increases for the linear motor. For all simulations shown \( l_2 = 0 \) as \( l_1 \) is varied. Data points and error bars are given by the mean and standard error across 100 independent simulations with \( 2 \times 10^8 \) time steps of size \( \Delta t = 5 \times 10^{-3} \).

III. DAMPING & TIME SCALES

We also investigated the motor’s performance at higher friction coefficients \( \gamma \) to ensure that the cause of the current reversal was not related to inertia. Many biological motor systems operate in low Reynolds number environments where viscous forces dominate inertia [1]. Increasing \( \gamma \) creates more particle drag, decreasing the effect of inertia. The results of these high \( \gamma \) simulations are shown in Fig. S3a for a circular motor as in Fig. 1b and in Fig. S3b for a linear motor as in Fig. 2c. As the friction increases the motor slows down, with the magnitude of current decreasing for all numbers of motifs. The current reversal observed at a large number of motifs, however, remains present, demonstrating the current reversal is not an inertial effect.

While the motor’s shuttling ring moves along a one-dimensional track, we emphasize that the friction coefficient is not the effective damping on a single degree of freedom representing the shuttling ring’s location. Rather, the friction explicitly acts on each particle. The ring’s motion emerges from many interactions of explicitly simulated particles, so it is possible for the ring’s motion to appear overdamped if it were to be reduced to a one-dimensional model even if...
the simulations are run with more modest $\gamma = 0.5$ damping acting on the particles. In that manner, some components like a free C particle may have some modest inertial memory even when other components have dynamics that are effectively overdamped.

To parse the impact of the friction coefficient, we determined the time scales of dynamical events (a time step, a bond vibration, free C diffusion, the damping time scale, ETC, FTC, and ring diffusion, transitions in the Markov models, catalyzed and uncatalyzed reactions, and net current) at three different friction coefficients: $\gamma = 0.5$, 10, and 25. These time scales, collected in Table S1, show that most events occur on time scales far longer than the damping time scale. At $\gamma = 0.5$, free C diffusion and bond vibrations still have mild inertial character, but the functional components of the motor move much more slowly than inertia is lost.

Estimates of the hierarchy of time scales in Table S1 came from a variety of analytical and computational methods. The damping time scale is given as $m/\gamma$ where $m$ is an individual particle mass of 1.0 for all particle types \[2\]. The bond vibration time scale was estimated as the inverse angular frequency of the harmonic spring connecting two tetrahedral particles $\sqrt{\mu_m/k}$ where $k = 120$ is the force constant and $\mu_m = 0.5$ is the reduced mass of the two particle system \[2\]. The C, ETC, FTC, and shuttling ring diffusive time scales were estimated by calculating their center of mass velocity autocorrelations and the Green-Kubo relation $D = \int_0^\infty dt \langle v_{\text{com}}(0) \cdot v_{\text{com}}(t') \rangle$. The velocity autocorrelations were collecting from simulations of a lone example of each species at $k_B T = 0.5$ with no GCMC moves and $2 \times 10^6$ time steps with the first $2 \times 10^5$ time steps discarded. To get the diffusion coefficient we numerically integrated the resulting autocorrelations with a trapezoidal rule with respect to $t'$ from 0 to 50, a time sufficient for all correlations to decay to negligible values. For FTC the procedure was repeated until a nonreactive trajectory was found. The shuttling ring was interlocked with a fixed linear track composed of only inert particles (no binding sites) and the diffusion calculation was restricted to the axial direction along the track ($x$-direction). The diffusive time scale was estimated as $L^2/D$ where $L$ was a characteristic length for each species. For C we estimated $L$ as the particle radius 0.45 \[2\]. For ETC and FTC we estimated $L$ as the centroid-to-vertex distance of a tetrahedron with a side length equal to two particle radii of 1.0 \[2\], $L \approx \sqrt{3}/2$. For the shuttling ring we estimated $L$ as the ring radius, where the circumference is approximated by the number of ring particles (12) multiplied by the approximate bond length (1.0), $L \approx 6/\pi$. The Markov transition time scales were simply the inverses of the Markov rates described in SI Sec. VI and shown in Fig. S4 for $\gamma = 0.5$. For Table S1 we report the values at $t_2 = 0$ and the minimum and maximum time scales across $l_1 = 0, 1, \ldots, 12$. The uncatalyzed and catalyzed reaction time scales are given as the average time between respective reactions where uncatalyzed reactions occur more than 2.0 units away from a catalytic site and catalyzed reactions occur within 2.0 units. These values were again averaged over all $l_1 = 0, 1, \ldots, 12$ for $l_2 = 0$. The current time scale is the time scale for the shuttling ring to have a net displacement of the size of a single track particle, essentially the inverse current. We used the current at $l_1 = 12$ for this time scale for each $\gamma$.

At $\gamma = 0.5$, damping occurs slower than the diffusive time scale for C, but faster than all other diffusive time scales and, most importantly, faster than any state transitions or currents associated with the motor. As $\gamma$ is increased the effect is a slowing of physical time scales like diffusion and motor operation and a quickening of the damping time scale. At $\gamma = 10.0$ and above even the diffusive motion of C is on a slower scale than the damping and the damping begins to act on the time scale of the fastest motions, the bond vibrations. Crucially, at all simulated $\gamma$ values the ring diffusion, reaction, motor transitions, and current occur on time scales much slower than the damping. While

| Time Scales | $\gamma = 0.5$ | $\gamma = 10$ | $\gamma = 25$ |
|------------|---------------|---------------|---------------|
| time step  | $5 \times 10^{-3}$ | $5 \times 10^{-3}$ | $5 \times 10^{-3}$ |
| bond vibration | $6 \times 10^{-2}$ | $6 \times 10^{-2}$ | $6 \times 10^{-2}$ |
| C diffusion  | $6 \times 10^{-2}$ | $10^0$ | $3 \times 10^0$ |
| damping     | $2 \times 10^0$ | $10^{-1}$ | $4 \times 10^{-2}$ |
| ETC diffusion | $2 \times 10^0$ | $4 \times 10^1$ | $10^2$ |
| FTC diffusion | $3 \times 10^0$ | $5 \times 10^1$ | $10^2$ |
| ring diffusion | $10^3$ | $2 \times 10^3$ | $3 \times 10^4$ |
| Markov transitions | $3 \times 10^2 - 3 \times 10^4$ | $10^2 - 6 \times 10^5$ | $7 \times 10^2 - 10^7$ |
| uncatalyzed reaction | $10^2$ | $10^2$ | $2 \times 10^2$ |
| catalyzed reaction | $3 \times 10^2$ | $2 \times 10^3$ | $5 \times 10^5$ |
| current | $8 \times 10^3$ | $8 \times 10^4$ | $3 \times 10^5$ |
| simulation | $10^6$ | $10^6$ | $10^6$ |
| Reynolds Numbers | $c = 1$ | $1 \times 10^{-5}$ | $6 \times 10^{-7}$ | $1 \times 10^{-7}$ |
| $c = 0.05$ | $7 \times 10^{-7}$ | $3 \times 10^{-8}$ | $7 \times 10^{-9}$ |
the underlying integration uses an underdamped Langevin method, this does not imply that the resulting dynamics are underdamped. Using an underdamped Langevin integrator with a large $\gamma$ can simply be more accurate and efficient than an overdamped Brownian integrator for equivalent dynamics [3], provided the underdamped integrator is $\gamma$-limit convergent [4]. Around $\gamma = 0.5$ some bulk diffusive processes may not be fully damped, but across all tested $\gamma$ values the motor itself is well damped. The slightly underdamped nature of the bulk at $\gamma = 0.5$ aids in keeping the nonequilibrium concentrations homogenous even though the moderating GCMC moves occur far from the motor toward the boundary of the simulations. For $\gamma > 25$ the physical processes occur on time scales too slow to tractably sample through simulation.

To confirm that the motor’s motion should be thought of as overdamped, we estimated the Reynolds number of the motor in our simulations. The Reynolds number is a dimensionless number that quantifies the relative strength of inertial and viscous effects, $Re = \rho v L/\mu$. Here $\rho$ is the fluid density, $v$ is velocity, $L$ is a characteristic length scale, and $\mu$ is the fluid viscosity. For our motors the velocity is the current (the net number of particles hops of the shuttling ring per time) and we selected the current at $l_2 = 0$ and $l_1 = 12$ as a characteristic example. As before, we estimated the characteristic length scale as the approximate radius of the shuttling ring $6/\pi$. We approximated the viscosity using the Stokes-Einstein relation $\mu = k_B T/(6\pi D L)$. As we are using a Langevin equation to approximate a solvent, there is no explicitly defined fluid density. We can set this density as some factor $c$ of the particle density of the shuttling ring particles $3m/(4\pi\sigma^3)$ where $m = 1$ is the shuttling ring particle mass and $\sigma = 1.0$ is the shuttling ring Lennard-Jones radius [2]. Conservatively, we can set $c = 1$, stating that the fluid and particle densities are equal. Studies of the Langevin equation, however, have suggested that it is valid in regimes where the fluid density is less than that of the explicit solute density, i.e. $c \approx 0.05$ [5]. Reynolds numbers in each case and for several $\gamma$ values are reported in Table S1. In all cases, even at $\gamma = 0.5$, we see that $Re \ll 1$, which implies that viscous forces dominate inertial forces and the motor is overdamped. Biological molecular motors in bulk water are estimated to have $Re \approx 10^{-8}$ [6]. Using values of 1000 kg/m$^3$ and $10^{-3}$ Pa s as the density and viscosity of water, a shuttling (benzylc amide) ring radius of 10 Å, and a current of about 100 Å per 12 hours, we estimate that the artificial molecular motor on which we based this model [7] has $Re \approx 10^{-16}$. While our model does not quite reach a biological Reynolds number and is far from that of the artificial molecular motor, it is nonetheless much less than unity, indicating that the motor is well damped and viscosity dominates any inertia.

In addition to an analysis of the damping, Table S1 confirms important time scale ordering critical to the motor’s operation. First, catalyzed reactions must occur faster than ring movement between binding sites. Without this, the ring’s position would not have a strong effect on the relative catalytic reaction rate between sites close to and far from the ring. This kinetic asymmetry is how the motor couples reactions to directed motion. At $\gamma = 0.5$ the catalyzed reaction time scale is faster than even the ring’s free diffusion along the track. This is not true at $\gamma = 10$ and $\gamma = 25$, however the catalyzed reaction time scale is still faster than the time scale for the shuttling ring to move from one binding site to another. This binding site hopping time scale is given roughly as $k_0 l_0^2$ (see SI Sec. IV for details) and is $9 \times 10^{-3}$ - $4 \times 10^0$ and $2 \times 10^4$ - $10^7$ for $\gamma = 10$ and $\gamma = 25$, respectively, compared to the catalyzed reaction time scales of $2 \times 10^3$ and $5 \times 10^3$, respectively. The motor clearly catalyzes reactions to create blocking groups faster than the shuttling ring moves between sites, allowing the shuttling ring to effectively inhibit blocking group creation nearby and generate current. Another important ordering is that of the reaction and diffusion. In order to effectively fuel the motor, the fuel diffusive time scale must be faster than the fuel reactive time scale or else fuel would decay before it ever reached the motor. This ordering is valid for all $\gamma$ values studied, but at $\gamma = 25$ the time scales get close with FTC diffusion happening at a time scale of $10^2$ and uncatalyzed reaction happening at a time scale of $2 \times 10^4$. The difference of time scales at $\gamma = 25$ is much smaller than lower $\gamma$ values and may be a reason why the current is much reduced at $\gamma = 25$, as a comparatively larger amount of fuel will decay in the bulk before ever reaching the motor. These time scale orderings match what is expected from the experimental system this model is based on [7]. Indeed, the model was built to satisfy these time scales so as to effectively generate current.

As the model was cast in non-dimensional form, we can set scales to examine how it maps onto physical systems. Suppose one wanted to construct one of these motors at the scale of colloids, where each simulated ball corresponds to a colloid whose interactions with the other colloids could be tuned, for example, through DNA coatings [8]. By choosing a particle radius, particle density, and temperature we can set the characteristic length scale, mass scale, and energy (time) scale, respectively. Table S2 shows some of the simulation results dimensionalized for reasonable scaling values for $\gamma = 0.5$ and $\gamma = 25$. Particle radii of 1 nm and 10 nm represent small and medium sized nanoparticles, respectively. Particle densities of 2 g/cm$^3$ and 20 g/cm$^3$ could represent moderate density (silica) and high density (metallic) nanoparticles, respectively. Temperatures of 275 K and 310 K represent cold water and body temperature, respectively. The $\gamma = 25$ simulations correspond to a physical situation. While the small, light particle/low temperature case implies somewhat large reaction rates and motor speeds, the large, heavy particle/high temperature case is reasonable in all values. The viscosities are now comparable to water (about 1.5 mPa s at 275 K and 0.7 mPa s at 310 K) or other common solvents and the reaction rate constant and motor cycling rate decrease to reasonable values, as well. In general, we see that the reaction rate constant is quite large when dimensionalized. This
TABLE S2. Dimensionalized model parameters and data.

| Chosen Scales | \( \gamma = 0.5 \) | \( \gamma = 25 \) |
|---------------|----------------|----------------|
| particle radius (nm) | 1 | 10 |
| particle density (g/cm\(^3\)) | 2 | 20 |
| temperature (K) | 275 | 300 |

| Dimensional Results | \( \gamma = 0.5 \) | \( \gamma = 25 \) |
|---------------------|----------------|----------------|
| total time (ms) | 0.03 | 30 |
| viscosity (mPa-s) | 0.01 | 0.7 |
| FTC concentration (mM) | 0.4 \( \times 10^{-4} \) | 0.3 \( \times 4 \times 10^{-3} \) |
| FTC → ETC + C rate constant (s\(^{-1}\)) | \( 2 \times 10^6 \) | \( 2 \times 10^6 \) | \( 2 \times 10^3 \) |
| motor cycling rate (Hz) | \( 2 \times 10^5 \) | 200 | 6 |
| C binding strength (kJ/mol) | 30 | 30 |

is not necessarily a problem, as it indicates that our fuel is relatively unstable relative to the other time scales in the system. A more stable fuel would increase the motor’s efficiency and as long as the relative time scale ordering is not disturbed (i.e. the catalyzed fuel reactions should still happen faster than ring cycling), the motor will still operate properly. The dimensionalized parameters for \( \gamma = 0.5 \) are less relevant if the free C is to be viewed as a colloidal particle. Using the Stokes-Einstein relation to extract the corresponding viscosity of the \( \gamma = 0.5 \) implicit solvent gives 0.01 mPa-s, a value that is too low for a reasonable liquid. Rather than representing a mesoscale complex built from colloids, the \( \gamma = 0.5 \) simulations are more reflective of situations where free C particles retain some inertia because their length scale approaches that of the solvent molecules. That the current reversal mechanism persists across the range of \( \gamma \) suggests that it has relevance for both the atomistic supramolecular scale and also mesoscale machines that could be build from colloidal particles.

IV. EXTENDED DISCUSSION OF THE MARKOV STATE MODELS

The data presented in Fig. 4b highlighted only those rates that directly contribute to shuttling ring motion. The Markov model described in Materials and Methods is parameterized by 24 additional rates involving the addition and removal of blocking groups. For the purposes of viewing those addition and removal rates as a function of \( l_1 \), it is convenient to not have to consider 24 different rates, motivating us to lump together multiple similar addition and removal processes. By “lump together”, we mean that we approximate the distinct transition as having identical rates (e.g., \( k_{01} = k_{24} = k_{35} = k_{07} \)). In Fig. S4a, this lumping manifests in multiple red edges describing the binding and unbinding of a blocking group adjacent to the shuttling ring, irrespective of whether other blocking groups are present at more distant sites. At large \( l_1 \) or \( l_2 \), the equivalence of these similar transitions is justified, but at small spacings it can start to break down. If the aim is to generate a Markov State Model that quantitatively reproduces the current for all spacings, the rate matrix in the main text is most appropriate (see Fig. S5). If, however, the aim is to see how these different attachment rates tend to depend on spacings, we find it very instructive to perform the lumping by forcing the rate matrix to take the form

\[
W = \begin{bmatrix}
-\Sigma_0 & k_{10} & k_{20} & k_{30} & 0 & 0 & 0 & 0 \\
0 & -\Sigma_1 & k_{11} & 0 & k_{20} & k_{30} & 0 & 0 \\
0 & 0 & -\Sigma_2 & k_{12} & k_{21} & 0 & k_{20} & 0 \\
0 & 0 & 0 & -\Sigma_3 & k_{13} & k_{22} & 0 & k_{20} \\
0 & k_{02} & k_{01} & 0 & -\Sigma_4 & 0 & k_{04} & k_{30} \\
0 & k_{03} & 0 & k_{01} & 0 & -\Sigma_5 & 0 & k_{20} \\
0 & 0 & k_{03} & k_{02} & k_{46} & 0 & -\Sigma_6 & k_{10} \\
0 & 0 & 0 & 0 & k_{03} & k_{02} & k_{10} & -\Sigma_7 \\
\end{bmatrix},
\]
FIG. S4.  (a) The 8-state Markov model of Fig. 4 with all states and rates shown.  (b) The populations of the Markov states (top) and the rates of allowed transitions between states (bottom) as a function of the $l_1$ spacing with $l_2 = 0$. The outline color of the state in (a) corresponds to its curve color in (b) (top) and the arrow color and line style (solid or dashed) for a transition in (a) corresponds to the same color and style in (b) (bottom). Data points and error bars are given by the mean and standard error across 100 independent simulations with $2 \times 10^8$ time steps of size $\Delta t = 5 \times 10^{-3}$.

obtained by setting

$$k_{03} = k_{15} = k_{26} = k_{47} = \frac{N_{03} + N_{15} + N_{26} + N_{47}}{\tau_0 + \tau_1 + \tau_2 + \tau_4}$$

$$k_{30} = k_{51} = k_{62} = k_{74} = \frac{N_{30} + N_{51} + N_{62} + N_{74}}{\tau_3 + \tau_5 + \tau_6 + \tau_7}$$

$$k_{02} = k_{14} = k_{36} = k_{57} = \tau_2 + \tau_1 + \tau_3 + \tau_5$$

$$k_{20} = k_{41} = k_{63} = k_{75} = \frac{N_{20} + N_{41} + N_{63} + N_{75}}{\tau_2 + \tau_4 + \tau_6 + \tau_7}$$

$$k_{01} = k_{24} = k_{35} = k_{67} = \frac{N_{01} + N_{24} + N_{35} + N_{67}}{\tau_0 + \tau_2 + \tau_3 + \tau_6}$$

$$k_{10} = k_{42} = k_{53} = k_{76} = \frac{N_{10} + N_{42} + N_{53} + N_{76}}{\tau_1 + \tau_4 + \tau_5 + \tau_7}.$$

As mentioned in Materials and Methods, $N_{ij}$ is the number of transitions from state $i$ to state $j$ and $\tau_i$ is the amount of time spent in state $i$, both calculated directly from simulated trajectories. At steady state $\frac{dp}{dt} = 0$ and the steady-state population of states is given by the normalized top eigenvector of $W$. We compare the empirical populations from simulation with the eigenvector populations in Fig. S5a. Those populations are identical at large $l_1$. For small $l_1$, the equivalence of lumped rates (e.g. $k_{03} = k_{15} = k_{26} = k_{47}$) breaks down, accounting for deviations between empirical and top-eigenvector populations.

Fig. S4a shows all the populations and lumped rates for the 8-state relative-frame Markov model with $l_2 = 0$, the motor that exhibits current reversal, and Fig. S6 shows the Markov state populations and rates for all $l_1$ and $l_2$ values. From Fig. S6, it is clear that populations and rates plateau as $l_1$ and $l_2$ grow large, demonstrating that the interesting changes that occur at small $l_1$ and $l_2$ are due to short-range steric effects. At large $l_1$ and $l_2$ spacing, the reaction events and shuttling ring position decouple, resulting in no current and rates independent of spacing.
FIG. S5. There is general agreement between the simulation and Markov models. Simulated empirical populations (a) and currents (b) (calculated as the net number of hops the shuttling ring makes per time) are plotted with solid lines. Corresponding data from the lumped-rate Markov model with $W$ are shown with dot-dashed lines, where the currents are computed using the steady-state probabilities as in Eq. 5. By lumping rates together into the Markov model with $W$, the model deviates at small $l_1$ (dot-dashed lines). Those deviations are rectified either by using the more general $W$ Markov model from from Eq. 3 of the main text (dashed lines) or by using empirical populations to compute currents across edges of a graph according to Eq. 7 (dotted lines). Data points and error bars are given by the mean and standard error across 100 independent simulations with $2 \times 10^8$ time steps of size $\Delta t = 5 \times 10^{-3}$.

V. ADDITIONAL STERIC MECHANISM DATA

In understanding the steric mechanisms that contribute to the motor’s current reversal, it is important to understand the range of these steric interactions. Fig. S7 shows both the interaction energy and force between a blue particle (part of ETC and FTC clusters) and a green particle (part of the shuttling ring) and also the interaction between a red particle (C) and a green particle. See Figs. 1a, 1b, and 2b for depictions of these particle types. From Fig. S7 we can see that the effective steric range between the shuttling ring and FTC/ETC is greater than the effective range between the shuttling ring and C. These distances are approximately 3 and 2 distance units, respectively, or about 3 and 2 particle radii.

Fig. 2 curiously shows that the linear motor’s current (defined as the net number of track particles traversed by the shuttling ring per time) continues to increase as the $l_1$ spacing increases. This data is reproduced in black in Fig. S8. If we instead examine the net number of jumps the shuttling ring makes between binding sites per time, shown in red in Fig. S8, we see that this value plateaus at large $l_1$. The increase in current at large $l_1$ is then due to the large distance the shuttling ring must traverse when making a jump between binding sites, which occurs at a rate independent of $l_1$. This current increase is then not due to additional or changing steric effects at large $l_1$, but simply the larger distance the ring must traverse between binding sites.

VI. SIMULATION DETAILS

We used both circular (Fig. 1b) and linear (Fig. 2a) tracks for the motor in this study. The details and derivations of the methods and models used here are presented elsewhere and, unless otherwise noted, the model parameters correspond to “Motor II” from that study [2].

The classical decomposition of a full tetrahedral cluster (FTC) into an empty tetrahedral cluster (ETC) and free central particle (C), depicted in Fig. 1a, provides the driving force for motor operation. The fuel was an FTC composed of a 4-particle tetrahedral cluster (blue) bound along its edges with harmonic potentials:

$$U_{\text{harmonic}}(r_{ij}) = \frac{1}{2}k_{ij}r_{ij}^2,$$

where $r_{ij}$ is the distance vector between tetrahedron particles and $k_{ij}$ is the harmonic force parameter. A free C
FIG. S6. The Markov state populations (a) and rates (b) for all combinations of $l_1$ and $l_2$ values studied. Populations and rates are plotted as a function of $l_1$ with different color curves denoting different values of $l_2$. Where possible rates in one direction along one edge of the Markov graph (Fig. S4) are plotted with the rates in the opposite direction along that edge using different line styles (solid and dashed). The population of state $i$ is labeled as $p_i$ and the transition rate from state $i$ to state $j$ is labeled as $k_{ij}$. The states $i$ and $j$ are numbered from 0 to 7 corresponding to the labels in Fig. S4a. Data points and error bars are given by the mean and standard error across 100 independent simulations with $2 \times 10^8$ time steps of size $\Delta t = 5 \times 10^{-3}$. 
FIG. S7. The modified, switched Lennard-Jones energy (a) and force (b) (given by (S6)) between a blue tetrahedron particle (TET) and a green shuttling ring particle (SHUTTLE), shown in blue, and between a red C particle (CENT) and a green shuttling ring particle (SHUTTLE), shown in red. The dashed gray lines in (b) represent the standard deviation of the zero-mean random force in the Langevin equation (Eq. 1) for comparison.

FIG. S8. Current (left axis, black) and net number of jumps between binding sites made by the shuttling ring (right axis, red) as a function of $l_1$ spacing in the linear motor for $l_2 = 0$. Data points and error bars are given by the mean and standard error across 100 independent simulations with $2 \times 10^8$ time steps of size $\Delta t = 5 \times 10^{-3}$.

particle (red) was inserted into this tetrahedron. To accommodate the C particle the cluster needs to deform from its equilibrium geometry, creating an entropically and energetically unfavorable state. To escape from the tetrahedral cage, the C particle must deform the geometry even further, resulting in an even higher free energy transition state, causing FTC to be metastable. Random thermal fluctuations can overcome this barrier, resulting in a transition to ETC + C.

The rotary motor with the circular track, depicted in Fig. 1b, consisted of two interlocked rings. Adjacent particles in each ring were connected with FENE bonds:

$$U_{\text{FENE}} = -\frac{1}{2} k_{F,ij} r_{\max,ij}^2 \log \left[ 1 - \left( \frac{|r_{ij}|}{r_{\max,ij}} \right)^2 \right], \quad \text{(S3)}$$

where $r_{ij}$ is the distance vector between neighboring ring particles $i$ and $j$ and $k_{F,ij}$ and $r_{\max,ij}$ are force and maximum extension parameters, respectively. Adjacent groups of three particles in the rings were also subject to an angular potential to maintain their circular geometry:

$$U_{\text{angle}}(\theta_{ijk}) = \frac{1}{2} k_{A,ijk} (\theta_{ijk} - \theta_{0,ijk})^2, \quad \text{(S4)}$$

where $\theta_{ijk}$ is the angle made by adjacent particles $i$, $j$, and $k$, and $k_{A,ijk}$ and $\theta_{0,ijk}$ are force and equilibrium angle parameters, respectively. The interlocked rings were free to diffuse around each other and within the simulation box. The smaller shuttling ring (green) consisted of 12 particles and the larger ring consisted of 32 particles. The linear motor, depicted in Fig. 2a, had the same 12-particle shuttling ring, but was then interlocked with a linear track of variable length that was fixed in place. The larger ring and the linear track were composed of shuttling ring binding sites (orange), catalytic sites (white), and inert (black) particles. Binding sites preferentially attracted the shuttling ring. Inert particles had no attractive interactions, they were purely volume excluding. The catalytic sites had attractive interactions with FTC particles that catalyze the FTC $\rightarrow$ ETC + C reaction.

In general, attractive and repulsive interactions between any two particles in the system were given by a modified
TABLE S3. Catalytic site-FTC modified Lennard-Jones interaction parameters.

| Particle Pair   | $\epsilon_A$ | $\epsilon_R$ |
|-----------------|--------------|--------------|
| CAT1-TET1       | 0.732877     | 0.888468     |
| CAT1-TET2       | 0.573471     | 1.215096     |
| CAT1-TET3       | 0.221362     | 1.424995     |
| CAT1-TET4       | 0.511311     | 0.216518     |
| CAT1-CENT       | 3.922903     | 2.798031     |
| CAT2-TET1       | 1.457497     | 1.147790     |
| CAT2-TET2       | 1.253230     | 1.440685     |
| CAT2-TET3       | 0.928847     | 2.063941     |
| CAT2-TET4       | 1.567248     | 3.788327     |
| CAT2-CENT       | 1.196286     | 1.421851     |

Lennard-Jones potential:

$$U_{LJ}(\mathbf{r}_{ij}) = 4\epsilon_{R,ij} \left( \frac{\sigma_{ij}}{|\mathbf{r}_{ij}|} \right)^{12} - 4\epsilon_{A,ij} \left( \frac{\sigma_{ij}}{|\mathbf{r}_{ij}|} \right)^{6},$$  \hspace{1cm} (S5)

where $\mathbf{r}_{ij}$ is the distance vector between particles $i$ and $j$, and $\epsilon_{R,ij}$, $\epsilon_{A,ij}$, and $\sigma_{ij}$ are attractive energy, repulsive energy, and interaction size parameters, respectively. This form of potential allowed us to change attraction and repulsion independently and every pairwise particle interaction was at least volume excluding ($\epsilon_R > 0$), but not necessarily attractive ($\epsilon_A \geq 0$). Practically, we evaluated these pairwise interactions using a cell list [9], where cell dimensions were no smaller than 4.25 on a side. The LJ interactions were then switched smoothly to 0 over the range $4.0 < |\mathbf{r}_{ij}| \leq 4.25$ to ensure that interactions did not extend beyond nearest neighbor cells. The switched LJ potential was

$$U_{\text{LJ\_switch}} = \begin{cases} 
U_{LJ}(\mathbf{r}_{ij}) & \text{if } |\mathbf{r}_{ij}| \leq 4.0 \\
U_{LJ}(\mathbf{r}_{ij})(1 + \lambda^2(2\lambda - 3)) & \text{if } 4.0 < |\mathbf{r}_{ij}| \leq 4.25 \\
0 & \text{if } |\mathbf{r}_{ij}| > 4.25,
\end{cases}$$  \hspace{1cm} (S6)

where $\lambda = (|\mathbf{r}_{ij}| - r_{\text{cut}} + r_{\text{switch}})/r_{\text{switch}}$, $r_{\text{cut}} = 4.25$, and $r_{\text{switch}} = 0.25$.

Most force field parameters for interactions between different particle types ($k_{F,ij}$, $r_{\text{max},ij}$, $k_{\theta,ijk}$, $\theta_{ijk}$, $k_{ij}$, $\epsilon_{R,ij}$, $\epsilon_{A,ij}$, and $\sigma_{ij}$) were identical to those of the “Motor II” parameterization in Ref. [2]. In the present study we introduced new attraction and repulsion LJ parameters between the catalytic site and the FTC particles. The previous study used three different types of catalytic particles (CAT1, CAT2, and CAT3) arranged CAT2-CAT1-CAT3 at each 3-particle catalytic site. Additionally, there were four distinct types of tetrahedron particles (TET1, TET2, TET3, and TET4). The specificity of these reactions was what led to the effective catalysis, but in the previous study this meant that the fuel-catalyst interactions were not symmetric. In the present study we sacrificed some specificity to symmetrize the catalyst, in order to make sure that catalyst asymmetry was not a confounding factor in the current reversal. The catalyst here consisted of only two types of catalyst particles (CAT2 and CAT1) arranged in a CAT2-CAT1-CAT2 configuration for each 3-particle catalytic site. The symmetrized FTC-catalyst interactions we used are given in Table S3.

The dynamics of the particles (excluding those of the linear track, which was fixed in place) were driven by a Langevin equation of motion. For a particle $i$ this equation is

$$\mathbf{r}_i = \frac{\mathbf{p}_i}{m_i},$$

$$\mathbf{p}_i = -\frac{\partial U(\mathbf{r})}{\partial \mathbf{r}_i} - \frac{\gamma}{m_i} \mathbf{p}_i + \xi_i,$$  \hspace{1cm} (S7)

where the potential energy $U$ is a function of all positions $\mathbf{r}$, $m_i$ is the particle’s mass, $\gamma$ is the friction coefficient and $\xi$ is a white noise satisfying $\langle \xi_i \rangle = 0$ and $\langle \xi_i(t)\xi_j(t') \rangle = 2\gamma k_B T \delta(t - t') \delta_{ij} \mathbf{I}$ at temperature $T$, where $\mathbf{I}$ is the identity
This equation was numerically integrated with the VRORV scheme \[10\]:

\[
\begin{align*}
p_i \left(t + \frac{1}{4}\Delta t\right) &= p_i(t) - \frac{\Delta t}{2} \frac{\partial U(r(t))}{\partial r_i(t)} \\
r_i \left(t + \frac{1}{2}\Delta t\right) &= r_i(t) + \frac{\Delta t}{2m_i} p_i \left(t + \frac{1}{4}\Delta t\right) \\
p_i \left(t + \frac{3}{4}\Delta t\right) &= e^{-\frac{m_i\Delta t}{2}} p_i \left(t + \frac{1}{4}\Delta t\right) + m_i \frac{1 - e^{-\frac{2m_i\Delta t}{\beta}}}{\beta} \eta_i \left(t + \frac{3}{4}\Delta t\right) \\
r_i \left(t + \Delta t\right) &= r_i \left(t + \frac{1}{2}\Delta t\right) + \frac{\Delta t}{2m_i} p_i \left(t + \frac{3}{4}\Delta t\right) \\
p_i \left(t + \Delta t\right) &= p_i \left(t + \frac{3}{4}\Delta t\right) - \frac{\Delta t}{2} \frac{\partial U(r(t + \Delta t))}{\partial r_i(t + \Delta t)}
\end{align*}
\] (S8)

where \(\eta_i\) is a random vector with components drawn from a zero mean, unity variance normal distribution and \(\beta = (k_B T)^{-1}\). The VRORV acronym reflects the order that dynamic variables are updated in each time step. First the velocity or momentum (V) is updated, then the position (R), then an Ornstein–Uhlenbeck (O) random process updates the velocity, then another position (R) update, and a final velocity or momentum (V) update. This procedure was repeated for \(N\) steps total time steps per simulation. Unless otherwise noted, the temperature was \(T = 0.5\), the time step was \(\Delta t = 0.005\), and the friction was set to \(\gamma = 0.5\). The simulations and models were non-dimensionalized with the energy scale set by the repulsion between inert (black) particles \(\epsilon_{R,\text{INERT}}\), the length scale set by the LJ radius of the inert particles \(\sigma_{\text{INERT}}\), and the mass scale set by the mass of the inert particles \(m_{\text{INERT}}\). The Boltzmann constant \(k_B\) was set to 1. All data are presented in terms of these reduced units.

For the rotary motor, the simulation cell consisted of two concentric cubic boxes with edge lengths \(L_{\text{inner}} = 30\) and \(L_{\text{outer}} = 34\). The motor rings were confined to the inner simulation box with a Lennard-Jones wall potential:

\[
U_{\text{wall}}(r_i) = 4\epsilon_{\text{wall}} \sum_{\alpha=x,y,z} \left( \left( \frac{\sigma_{\text{wall}}}{r_{\alpha,i} - \frac{1}{2}L_{\text{inner}}} \right)^{12} + \left( \frac{\sigma_{\text{wall}}}{r_{\alpha,i} + \frac{1}{2}L_{\text{inner}}} \right)^{12} \right),
\] (S9)

where \(r_i\) is a motor particle, \(\epsilon_{\text{wall}} = 1\) and \(\sigma_{\text{wall}} = 1\) are wall energy and size parameters, respectively. Particles of the FTC, ETC, and C species did not interact with the wall potential, allowing them to diffuse freely between the inner and outer boxes. The faces of the outer box were periodic, allowing the species to exit one face of the box and immediately re-enter through the opposite face. The box dimensions equate to an inner volume (accessible to the motor) of \(V_{\text{inner}} = 27000.0\), a total volume of \(V_{\text{outer}} = 39304.0\), and a volume available for GCMC moves of \(V_{\text{GCMC}} = V_{\text{outer}} - V_{\text{inner}} = 12304.0\).

For the linear motor, the track was fixed in position, centered in the \(yz\)-plane at \((y = 0, z = 0)\) with a spacing of \(d = 0.992\) between track particles, the approximate equilibrium distance between particles in the large ring of the rotary motor. As depicted in Fig. 2, the inner and outer simulation boxes were no longer necessarily cubic and they shared boundaries in the \(yz\)-plane. The shared inner and outer box lengths in the \(x\)-direction \(L_x\) were determined by the size of linear motor itself, \(L_x = dN\text{motif}(l_1 + l_2 + 4)\) (where there were \(l_1 + l_2\) inert particles, 3 catalytic particles, and 1 binding particle per repeat unit). The shared end faces were then both periodic allowing FTC, ETC, C, and the shuttling ring to cross. In this way the shuttling ring diffused on an effectively infinite linear track. The remaining \(y\) and \(z\) dimensions of the inner and outer box were set so that the \(y\) and \(z\) dimensions were equivalent and that \(V_{\text{inner}} = 27000.0\) and \(V_{\text{GCMC}} = 12304.0\), for consistency with the rotary motor. By keeping these volumes consistent across all simulations and all configurations, we ensured that concentrations, free energies, and shifted chemical potentials were equivalent across all simulations. We calculated \(L_{y,\text{inner}} = L_{z,\text{inner}} = \sqrt{V_{\text{inner}}/L_x}\) and \(L_{y,\text{outer}} = L_{z,\text{outer}} = \sqrt{(V_{\text{inner}} + V_{\text{GCMC}})/L_x}\). For completeness we still implemented a wall potential in the \(y\) and \(z\) directions applied to the shuttling ring (although the shuttling ring was mechanically interlocked with the central track, making it impossible to approach the wall):

\[
U_{\text{wall}}(r_i) = 4\epsilon_{\text{wall}} \sum_{\alpha=y,z} \left( \left( \frac{\sigma_{\text{wall}}}{r_{\alpha,i} - \frac{1}{2}L_{\alpha,\text{inner}}} \right)^{12} + \left( \frac{\sigma_{\text{wall}}}{r_{\alpha,i} + \frac{1}{2}L_{\alpha,\text{inner}}} \right)^{12} \right),
\] (S10)
where $r_i$ is a shuttling ring particle, and $\epsilon_{\text{wall}} = 1$ and $\sigma_{\text{wall}} = 1$, as before.

Periodically we performed GCMC insertion and deletion moves of the FTC, ETC, and C species in the space between the inner and outer boxes [9]. GCMC moves were attempted every 100 Langevin time steps. By keeping the motor spatially separated from the GCMC moves, we ensured that these instantaneous changes did not directly affect the motor’s dynamics. For each GCMC move we selected randomly between the six possible moves (insertion or removal of FTC, ETC, and C) with uniform probability. For insertion moves, the momenta of the inserted species were drawn from a Boltzmann distribution and for FTC and ETC their positions were drawn from a pre-sampled canonical library of $10^4$ configurations [11, 12]. The subsequent acceptance probabilities for GCMC insertion moves and removal moves of species $i$, respectively, are:

$$P_{\text{acc}, i, \text{insertion}}(r', p' \rightarrow r, p) = \min \left[ 1, \frac{1}{N_i(r')} e^{-\beta(U(r') - U(r) - U_0^i - \mu_i')} \right]$$

and

$$P_{\text{acc}, i, \text{removal}}(r', p' \rightarrow r, p) = \min \left[ 1, N_i(r) e^{-\beta(U(r) - U(r') + U_0^i + \mu_i')} \right],$$

where $r$ and $p$ are the positions and momenta of the initial configuration, $r'$ and $p'$ are the positions and momenta of the trial configurations, $N_i$ is the number of molecules of species $i$, $U(r)$ is the potential energy of the initial configuration, $U(r')$ is the potential energy of the trial configuration, $U_0^i$ is the internal potential energy of the isolated molecule being inserted or removed, and $\mu_i'$ is the relative chemical potential. The relative chemical potential is the true chemical potential less the Helmholtz free energy of a single isolated species of $i$ in the same volume, $\mu_i' = \mu_i - A_0^i$. Unless otherwise noted, these external relative chemical potentials were set to $\mu_{\text{FTC}}' = 0.5$, $\mu_{\text{ETC}}' = -10.0$, and $\mu_C' = -10.0$. These values ensured that FTC tended to be inserted while ETC and C tended to be removed, resulting in a nonequilibrium concentration of FTC and practically no free ETC and C in the simulation cell.

[1] R. D. Astumian, Physical Chemistry Chemical Physics 9, 5067 (2007).
[2] A. Albaugh and T. R. Gingrich, Nature Communications 13, 2204 (2022).
[3] A. Ladd, Lectures at the 3rd Warsaw School of Statistical Physics (Kazimierz, Poland) [http://www.che.ufl.edu/ladd/publications/kmz-09.pdf] (2009).
[4] B. Leimkuhler, D. Paulin, and P. A. Whalley, arXiv preprint arXiv:2302.10684 (2023).
[5] D. Heyes and A. Brañka, Molecular Physics 96, 1757 (1999).
[6] A. I. Brown and D. A. Sivak, Chemical Reviews 120, 434 (2019).
[7] M. R. Wilson, J. Solà, A. Carlone, S. M. Goldup, N. Lebrasseur, and D. A. Leigh, Nature 534, 235 (2016).
[8] S. Angioletti-Uberti, B. M. Mognetti, and D. Frenkel, Physical Chemistry Chemical Physics 18, 6373 (2016).
[9] D. Frenkel and B. Smit, Understanding Molecular Simulation: From Algorithms to Applications, Vol. 1 (Elsevier, 2001).
[10] J. Fass, D. A. Sivak, G. E. Crooks, K. A. Beauchamp, B. Leimkuhler, and J. D. Chodera, Entropy 20, 318 (2018).
[11] A. Gupta, L. A. Clark, and R. Q. Snurr, Langmuir 16, 3910 (2000).
[12] S. Chempath, L. A. Clark, and R. Q. Snurr, The Journal of Chemical Physics 118, 7635 (2003).