

Supporting Information:

**Nonequilibrium Energy Transduction in
Stochastic Strongly Coupled Rotary Motors**

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Current under tight coupling

The Langevin equations describing the full system are

$$\zeta \dot{\theta}_o + \frac{n_o}{2} E_o \sin n_o(\theta_o - \phi) + \frac{1}{2} E_{\text{couple}} \sin(\theta_o - \theta_1) - \mu_{H^+} = \eta_{\theta_o}, \quad (\text{S1})$$

$$\zeta \dot{\theta}_1 + \frac{n_1}{2} E_1 \sin n_1 \theta_1 - \frac{1}{2} E_{\text{couple}} \sin(\theta_o - \theta_1) - \mu_{\text{ATP}} = \eta_{\theta_1}, \quad (\text{S2})$$

with the noise having statistics that satisfy

$$\langle \eta_i(t) \eta_j(t') \rangle = 2\zeta k_B T \delta_{ij} \delta(t - t'). \quad (\text{S3})$$

Here, over-dots denote a time derivative. We impose identical friction coefficients ζ .

We consider the case of equal numbers of energy barriers in each subsystem, $n_o = n_1 = n$. Summing (S1) and (S2), dividing by two, and substituting $\theta_o = \theta_1 = \theta$ (in the infinite-coupling limit of $E_{\text{couple}} \rightarrow \infty$, the subsystems maintain the same angle), gives

$$\zeta \dot{\theta} + \frac{n}{4} E_o \sin n(\theta - \phi) + \frac{n}{4} E_1 \sin n\theta - \frac{1}{2} (\mu_{H^+} + \mu_{\text{ATP}}) = \eta_{\theta}, \quad (\text{S4})$$

where the composite noise term η_{θ} satisfies

$$\langle \eta_{\theta}(t) \eta_{\theta}(t') \rangle = \zeta k_B T \delta(t - t'). \quad (\text{S5})$$

The resulting one-dimensional energy landscape is

$$V(\theta) = -\frac{1}{4} E_o \cos n(\theta - \phi) - \frac{1}{4} E_1 \cos n\theta \quad (\text{S6a})$$

$$= -\frac{1}{4} E \cos n(\theta - \varphi), \quad (\text{S6b})$$

for

$$E \equiv \sqrt{E_o^2 + E_1^2 + 2E_o E_1 \cos n\phi} , \quad (\text{S7})$$

$$\tan n\varphi \equiv \frac{\sin n\phi}{\frac{E_o}{E_1} + \cos n\phi} . \quad (\text{S8})$$

The chemical driving force exerted on the one-dimensional system is $\mu \equiv \frac{1}{2}(\mu_{\text{H}^+} + \mu_{\text{ATP}})$.

The exact expression for the average probability current is:¹

$$\langle \mathcal{J} \rangle = \frac{k_B T}{\zeta} \left[(1 - e^{-2\pi\beta\mu})^{-1} \int_0^{2\pi} d\theta e^{\beta U(\theta)} \int_0^{2\pi} d\theta' e^{-\beta U(\theta')} - \int_0^{2\pi} d\theta e^{-\beta U(\theta)} \int_0^\theta d\theta' e^{\beta U(\theta')} \right]^{-1} , \quad (\text{S9})$$

We integrate this numerically, using Mathematica's NIntegrate function with the ‘‘DoubleExponential’’ method. $U(\theta) \equiv V(\theta) - \mu\theta$ is the combination of the underlying energy landscape and the chemical driving force. We note that when the number of energy barriers is not equal ($n_o \neq n_1$), this result can still be used; the only difference lies in the energy landscape $V(\theta)$, which generally does not simplify as in (S6b).

In the limit of small energy barriers compared to the chemical driving force ($n_o E_o, n_1 E_1 \ll \frac{1}{2}(\mu_{\text{H}^+} + \mu_{\text{ATP}})$), also referred to as the case of no energy barriers, (S4) reduces to

$$\zeta \dot{\theta} - \frac{1}{2}(\mu_{\text{H}^+} + \mu_{\text{ATP}}) = \eta_\theta , \quad (\text{S10})$$

which describes diffusion subject to a constant force $\frac{1}{2}(\mu_{\text{H}^+} + \mu_{\text{ATP}})$. Integrating (S10) over fluctuations gives the average drift velocity

$$\langle \dot{\theta} \rangle = \frac{\mu_{\text{H}^+} + \mu_{\text{ATP}}}{2\zeta} . \quad (\text{S11})$$

Finally, output power is $\mathcal{P}_{\text{ATP}} = -\mu_{\text{ATP}} \langle \dot{\theta} \rangle = -2\pi\mu_{\text{ATP}} \langle \mathcal{J} \rangle$.

Current in the absence of energy barriers

Starting from the dynamical equations for the full two-dimensional system (S1,S2), consider the limit of energy barriers much smaller than the chemical driving forces ($n_o E_o \ll \mu_{H^+}$, $n_1 E_1 \ll \mu_{ATP}$), leading to

$$\zeta \dot{\theta}_o + \frac{1}{2} E_{\text{couple}} \sin(\theta_o - \theta_1) - \mu_{H^+} = \eta_{\theta_o} , \quad (\text{S12})$$

$$\zeta \dot{\theta}_1 - \frac{1}{2} E_{\text{couple}} \sin(\theta_o - \theta_1) - \mu_{ATP} = \eta_{\theta_1} . \quad (\text{S13})$$

Summing and subtracting these equations, and changing variables to the mean

$$\bar{\theta} \equiv \frac{1}{2}(\theta_o + \theta_1) , \quad (\text{S14})$$

and relative angle

$$\Delta\theta \equiv \frac{1}{2}(\theta_o - \theta_1) , \quad (\text{S15})$$

uncouples (S12,S13) to give independent Langevin equations:

$$\zeta \partial_t \bar{\theta} - \frac{1}{2}(\mu_{H^+} + \mu_{ATP}) = \eta_{\bar{\theta}} , \quad (\text{S16})$$

$$\zeta \partial_t \Delta\theta + \frac{1}{2} E_{\text{couple}} \sin 2\Delta\theta - \frac{1}{2}(\mu_{H^+} - \mu_{ATP}) = \eta_{\Delta\theta} . \quad (\text{S17})$$

The transformed noise terms $\eta_{\bar{\theta}} \equiv \frac{1}{2}(\eta_{\theta_o} + \eta_{\theta_1})$ and $\eta_{\Delta\theta} \equiv \frac{1}{2}(\eta_{\theta_o} - \eta_{\theta_1})$ each satisfy

$$\langle \eta(t) \eta(t') \rangle = \zeta k_B T \delta(t - t') . \quad (\text{S18})$$

(S16) can be integrated directly, exactly like (S10). (S17) is analogous to (S4) in the sense that both are Langevin equations describing a system subject to a periodic energy landscape and a constant driving force. An exact expression for the probability current can be derived

using (S9), where $U(\theta) = -\frac{1}{4}E_{\text{couple}} \cos 2\theta - \mu\theta$ and $\mu = \frac{1}{2}(\mu_{\text{H}^+} - \mu_{\text{ATP}})$. The system is now reduced to one dimension with energy landscape $U(\theta)$ and an externally set chemical driving force μ . Linearly combining these probability currents gives each subsystem's probability current:

$$\langle \mathcal{J}_0 \rangle = \langle \mathcal{J}_{\bar{\theta}} \rangle + \langle \mathcal{J}_{\Delta\theta} \rangle, \quad (\text{S19})$$

$$\langle \mathcal{J}_1 \rangle = \langle \mathcal{J}_{\bar{\theta}} \rangle - \langle \mathcal{J}_{\Delta\theta} \rangle. \quad (\text{S20})$$

Output power is $\mathcal{P}_{\text{ATP}} = -\mu_{\text{ATP}} \langle \dot{\theta}_1 \rangle = -2\pi\mu_{\text{ATP}} \langle \mathcal{J}_1 \rangle$.

Power-maximizing coupling

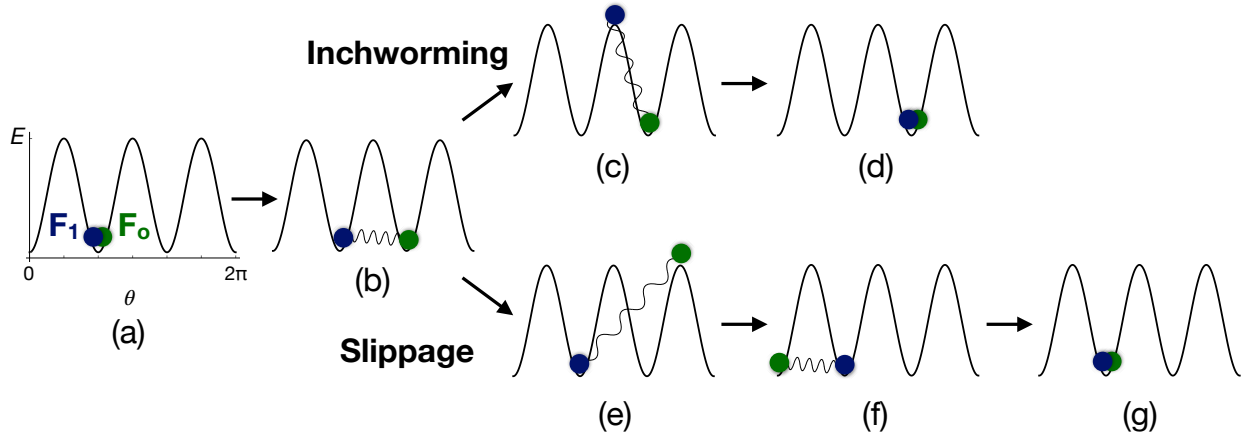


Figure S1: Visualization of inchworming and slippage. F_0 and F_1 start in the same state (a), then F_0 advances to the next state (b). Inchworming, which leads to energy transduction, involves F_1 advancing to catch up with F_0 (c-d). Slippage occurs when F_0 further advances to the next state (e-f), after which it is likely to continue on to complete a full cycle (g). Throughout, $n = 3$ and there is no phase offset. Landscape tilts are omitted to simplify depiction.

Here we present a simple theory to predict the coupling at which output power is maximized, by approximating its two components (input power and efficiency) in terms of the rates of the rate-limiting steps for energy transduction and slippage. We restrict our attention to $n = 3$ metastable states, no phase offset, and the regime of biological interest where

the proton driving force is greater than and opposite in sign to the ATP driving force.

For significant coupling, F_o and F_1 are frequently in the same state (Fig. S1a). For tight coupling, F_o and F_1 must cross a barrier simultaneously; but for somewhat weaker coupling, the most likely event from this configuration is F_o moving ahead to the next state (Fig. S1b). From there, the two most likely events are ‘inchworming’ where F_1 catches up to F_o (Fig. S1c-d) or ‘slippage’ where F_o moves further ahead (Fig. S1e-f), from which F_o will most likely continue further to its original position (Fig. S1g-h) without F_1 having moved.

The rates $r = r_0 e^{-\beta \Delta E}$ of these competing steps are proportional to the exponentials of the respective energy barriers (Fig. S1c,e). The rate-limiting step for inchworming (Fig. S1b→c) has rate

$$r_{\text{inch}} = r_0 \exp \left\{ -\beta \left[E_1 - \frac{1}{2} E_{\text{couple}} - \frac{\pi}{3} \mu_{\text{ATP}} \right] \right\} . \quad (\text{S21})$$

The inchworming rate increases with decreasing barrier height, increasing coupling strength, or increasing ATP driving force. The rate-limiting step for slippage (Fig. S1b→e) has rate

$$r_{\text{slip}} = r_0 \exp \left\{ -\beta \left[E_o + \frac{1}{4} E_{\text{couple}} - \frac{\pi}{3} \mu_{\text{H}^+} \right] \right\} . \quad (\text{S22})$$

The slippage rate increases with decreasing barrier height, decreasing coupling strength, or increasing proton driving force.

The ratio of inchworming and slippage rates is

$$\frac{r_{\text{slip}}}{r_{\text{inch}}} = \exp \left\{ \beta \left[E_1 - E_o + \frac{\pi}{3} (\mu_{\text{H}^+} - \mu_{\text{ATP}}) - \frac{3}{4} E_{\text{couple}} \right] \right\} . \quad (\text{S23})$$

For identical F_o and F_1 barrier heights, this reduces to

$$\frac{r_{\text{slip}}}{r_{\text{inch}}} = \exp \left\{ \beta \left[\frac{\pi}{3} (\mu_{\text{H}^+} - \mu_{\text{ATP}}) - \frac{3}{4} E_{\text{couple}} \right] \right\} . \quad (\text{S24})$$

The slippage-inchworming ratio increases with decreasing coupling strength and with increasing magnitude of driving forces (i.e., more positive μ_{H^+} or more negative μ_{ATP}). Notice that barrier height has an identical effect on both rates, so cancels out when comparing the two.

One inchworm event rotates the joint system 1/3 of a full cycle, whereas one slippage event results in a full cycle of slip, so the efficiency is simply expressed in terms of the rate ratio,

$$\frac{\eta}{\eta_{\max}} = \frac{\frac{1}{3}r_{\text{inch}} - r_{\text{slip}}}{\frac{1}{3}r_{\text{inch}}} \quad (\text{S25})$$

$$= 1 - 3\frac{r_{\text{slip}}}{r_{\text{inch}}} . \quad (\text{S26})$$

Substituting (S24) gives the efficiency as a function of the coupling strength,

$$\frac{\eta}{\eta_{\max}} = 1 - 3 \exp \left\{ \beta \left[\frac{\pi}{3} (\mu_{H^+} - \mu_{ATP}) - \frac{3}{4} E_{\text{couple}} \right] \right\} . \quad (\text{S27})$$

Figure S2 shows that this simple theory accurately predicts the coupling at which efficiency begins to drop, across the examined variation of driving forces.

For strong proton driving force, F_o backsteps are negligible, and for intermediate-or-stronger coupling, the slowest step is F_o stepping one state ahead of F_1 (Fig. S1a→b). Hence the (net) input power is simply proportional to the exponential of the activation energy of this slowest step,

$$\mathcal{P}_{H^+} \propto \exp \left\{ -\beta \left[\frac{1}{4} E_{\text{couple}} + E_o - \frac{\pi}{3} \mu_{H^+} \right] \right\} . \quad (\text{S28})$$

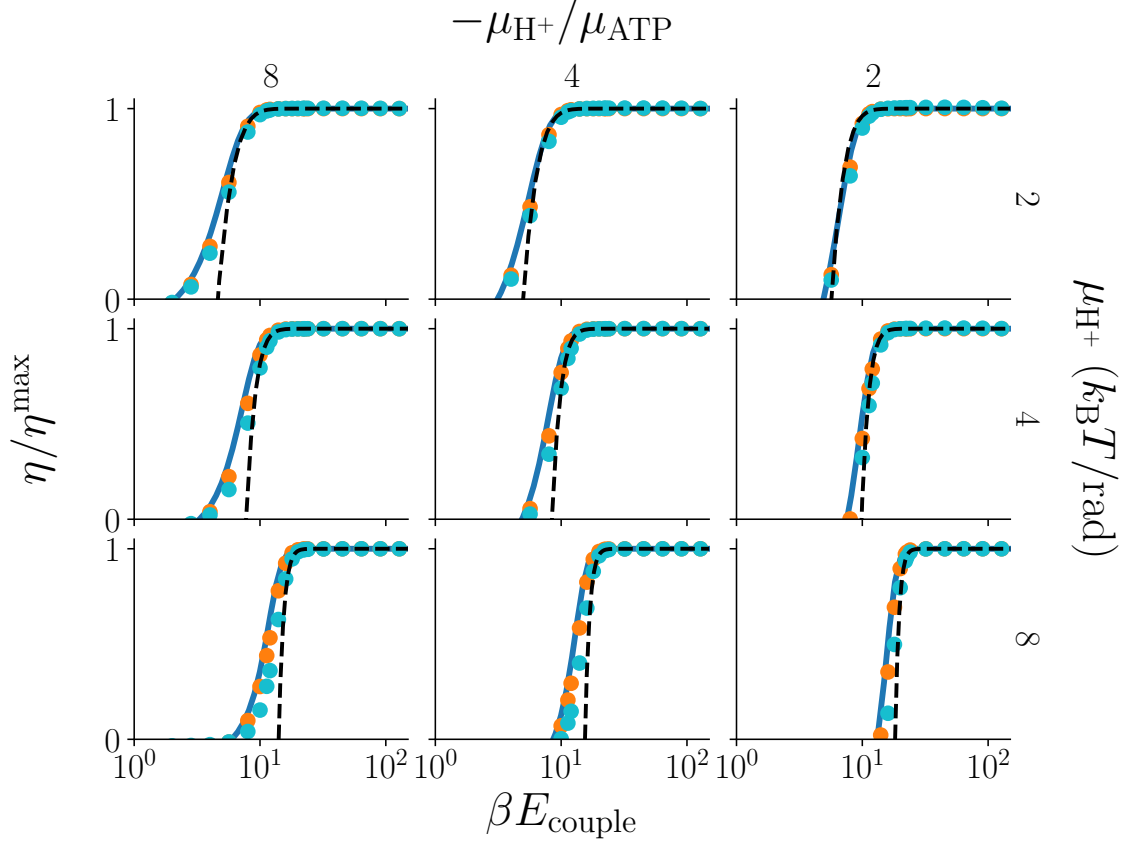


Figure S2: Scaled efficiency as a function of coupling strength, for no barriers (blue curve), simulated for barrier heights $\beta E_o = \beta E_1 = 2$ (orange circles) or 4 (light blue circles), and for simple theory (Eq. (S27), dashed black curve).

Thus the output power is

$$\mathcal{P}_{\text{ATP}} = -\frac{\eta}{\eta_{\text{max}}} \mathcal{P}_{\text{H}^+} \quad (\text{S29})$$

$$\propto \exp \left\{ -\frac{1}{4} \beta E_{\text{couple}} \right\} - 3 \exp \left\{ \beta \left[\frac{\pi}{3} (\mu_{\text{H}^+} - \mu_{\text{ATP}}) - E_{\text{couple}} \right] \right\} . \quad (\text{S30})$$

This predicts that output power is maximized at coupling strength

$$\beta E_{\text{couple}}^* = \frac{4}{3} \ln 12 + \frac{4\pi}{9} \beta (\mu_{\text{H}^+} - \mu_{\text{ATP}}) . \quad (\text{S31})$$

This aligns with intuition: increasing either the driving force on F_o (more positive μ_{H^+}) or the resistive force on F_1 (more negative μ_{ATP}) increases the slip between subsystems,

hence the optimal coupling (that maximizes inter-subunit flexibility subject to only minimal slippage) shifts higher. Figure 3 in the main text shows that this prediction closely approximates the power-maximizing coupling in full numerical simulations.

Computational methods

All numerical code is freely available at Github.²

Steady-state condition

We initialize in the standard Gibbs-Boltzmann equilibrium distribution,

$$P(\theta_o, \theta_1, t = 0) \propto \exp \{ -\beta V(\theta_o, \theta_1) \} . \quad (\text{S32})$$

We numerically integrate the 2D Fokker-Planck equation (see main text) with periodic boundary conditions using standard finite-difference methods.³ This evolves the joint probability distribution from a specified initial distribution to the steady-state distribution $P_{\text{ss}}(\theta_o, \theta_1)$. Convergence to steady state is judged by the distribution remaining unchanged after evolution for $\Delta t = 10^{-3}$, as measured by the total variation distance:

$$\frac{1}{2} \iint d\theta_o d\theta_1 |P_{\text{ss}}(\theta_o, \theta_1, t + \Delta t) - P_{\text{ss}}(\theta_o, \theta_1, t)| < 10^{-16}. \quad (\text{S33})$$

Setting the time scale

We assign physical units by equating the simulation timescale and the physical timescale for analogous experiments. We approximate ATP synthase as a sphere rotating around an axis through its center. The rotational drag coefficient for a sphere of radius r rotating in a fluid

of viscosity η is

$$\zeta_r = 8\pi\eta r^3 . \quad (\text{S34})$$

The viscosity of water is 10^{-9} pN s nm $^{-2}$, and ATP synthase has a radius ~ 15 nm. The diffusion coefficient is found using the Einstein relation,

$$D_{\text{phys}} = \frac{k_{\text{B}}T}{\zeta_r}, \quad (\text{S35})$$

where k_{B} is Boltzmann's constant, and $T = 300$ K is room temperature. The ratio of physical diffusion coefficient to simulation diffusion coefficient is

$$\frac{D_{\text{phys}}}{D_{\text{sim}}} = \frac{1.9 \cdot 10^6}{10^{-3}} \frac{\text{rad}^2 \text{s}^{-1}}{\Delta\theta^2 \Delta t^{-1}}, \quad (\text{S36})$$

for simulation grid spacing $\Delta\theta = \pi/180$ rad and simulation timescale Δt . Setting this ratio to unity implies that the simulation timestep corresponds to

$$\Delta t = 6.7 \cdot 10^{-5} \text{ s} . \quad (\text{S37})$$

Number of energy barriers

Varying $n_o = n_1$

Here we vary the number of energy barriers, with the constraint $n_o = n_1$. Figure S3 shows output power and efficiency as a function of coupling strength for various numbers of barriers. The output power curves in Fig. S3a are similar to those in the main text. In particular, the curve of orange circles is identical to the case studied there. Every curve in Fig. S3a shows a maximum at some intermediate-strength coupling. The peak is the most dramatic for six barriers, but quite subtle for a single barrier. The efficiency, shown in Fig. S3b, varies little

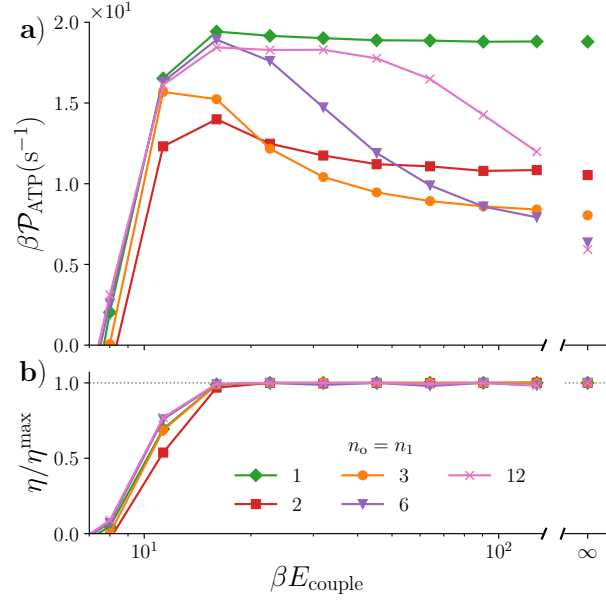


Figure S3: a) Output power as a function of coupling strength βE_{couple} , for different numbers of barriers, with $n_o = n_1$, no phase offset, barrier heights $\beta E_o = \beta E_1 = 2$, and chemical driving forces $\mu_{H^+} = 4 k_B T / \text{rad}$ and $\mu_{\text{ATP}} = -2 k_B T / \text{rad}$. b) Efficiency under the same conditions, scaled by the theoretical maximum efficiency $\eta^{\text{max}} \equiv -\mu_{\text{ATP}} / \mu_{H^+}$. Horizontal grey dotted line: maximum efficiency. Infinite coupling values are calculated using (S9).

with the number of barriers.

Compared to the $n_o = n_1 = 3$ result (orange circles in this plot), the output power for more barriers has a higher peak. The more barriers, the easier it is for one of the subsystems to diffuse ahead to a subsequent minimum since the subsystems can remain closer together, incurring a smaller ‘penalty’ from the energetic coupling term. This also leads to wider peaks at these coupling strengths. Moreover, when there is only a single minimum (and hence single barrier), it is counterproductive for F_o to jump ahead, since it would end up in the same minimum again. This introduces slippage and reduced output power and efficiency. It should be noted that a landscape with the prescribed barrier height, chemical driving force, and a single barrier actually does not have a local minimum. This leads to the green diamond curve being similarly shaped to the barrier-less case, which does not have a maximum at intermediate-strength coupling.

Figure S4 shows (a) output power and (b) efficiency as a function of the scaled phase offset

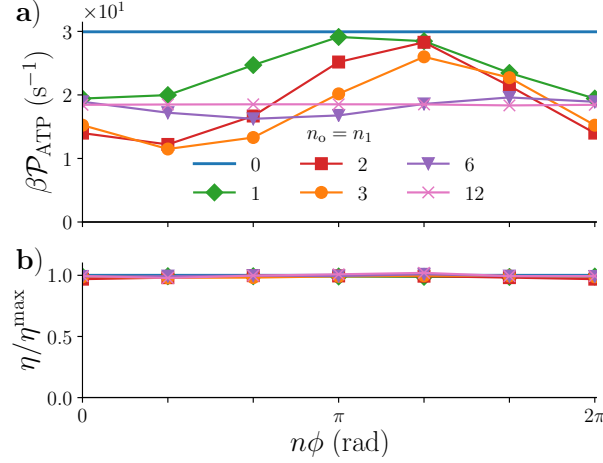


Figure S4: a) Output power as a function of scaled phase offset $n\phi$ between the subsystems with various numbers of barriers $n_o = n_1$, at coupling strengths $\beta E_{\text{couple}} = 16$, barrier heights $\beta E_o = \beta E_1 = 2$, and chemical driving forces $\mu_{\text{H}^+} = 4 k_{\text{B}}T/\text{rad}$ and $\mu_{\text{ATP}} = -2 k_{\text{B}}T/\text{rad}$. b) Efficiency under the same conditions, scaled by the theoretical maximum efficiency.

$n\phi$, for various numbers of minima. The phase offset is scaled by a factor of $n_o = n_1 = n$ to compare one period across all curves. The output power varies as a function of the phase offset, though this variation is minimal for $n_o = n_1 = 12$. More barriers lead to smaller variation in output power. More barriers means F_1 must overcome a smaller barrier height in a single hop to the next metastable state, since the tilt of the landscape stays the same. This leads to the effective barrier height decreasing, resulting in less variation in output power as the phase offset is varied. At the same time, as more barriers are introduced the system slows down because there are more barriers to overcome. The opposite is seen for fewer barriers: $n_o = n_1 = 2$ has greater variation in output power, and the peak power is somewhat higher. Effectively, a lower coupling strength is needed for a system with fewer barriers to approach the infinite-coupling power.

A single barrier, $n_o = n_1 = 1$, leads to output power that varies slightly less with phase offset, but higher peak output power. This is likely a consequence of the landscape not having any local minima at these parameters.

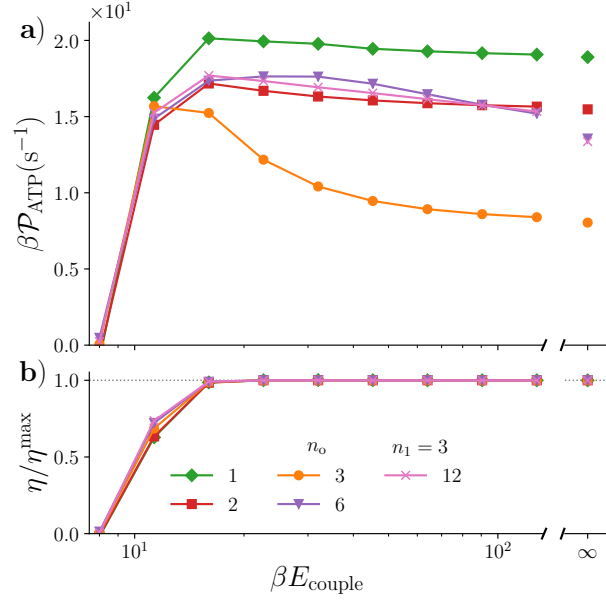


Figure S5: a) Output power and efficiency as a function of coupling strength βE_{couple} with various numbers of barriers n_o , while keeping $n_1 = 3$ fixed. There is no phase offset, barrier heights are $\beta E_o = \beta E_1 = 2$, and chemical driving forces are $\mu_{\text{H}^+} = 4 k_{\text{B}}T/\text{rad}$ and $\mu_{\text{ATP}} = -2 k_{\text{B}}T/\text{rad}$. b) Efficiency under the same conditions, scaled by the theoretical maximum efficiency. Horizontal grey dotted line: maximum efficiency.

Varying n_o

Figure S5 shows output power as a function of coupling strength for a varying number of F_o barriers, with 3 F_1 barriers. For all n_o , output power is maximized at intermediate-strength coupling. The peak in output power is by far the most pronounced when $n_o = 3$ (orange circles), when the energy barriers in F_o and F_1 align and hence the trade-off is greatest between minimizing slip and loosening coupling sufficiently to capitalize on random fluctuations. When $n_o \neq n_1$, not all landscape barriers align with a landscape barrier of the other subsystem, leading to smaller effective barriers compared to the infinite-coupling limit. Smaller peaks are easier to jump over, consequently they do not restrict the optimal coupling strength to the same degree.

Barrier heights

Once the barrier heights are sufficiently large to (in combination with tilts from driving forces) prevent any significant fraction of back steps, the output power is simply proportional to the rate of forward steps, and hence proportional to the exponential of the barrier height, $\exp[-\beta E^\ddagger]$. In this regime, the output power of any machine (regardless of driving forces and coupling strength) decreases with barrier height according to the same exponential decay. Thus once back steps are negligible, the ordering of machines by output power—and more specifically the coupling that optimizes output power—does not vary with barrier height. This physical intuition can be confirmed for tightly coupled subsystems, when the power is simply calculable by numerical integration (proportional to Eq. (S9)), permitting systematic exploration of its dependence on barrier height.

Figure S6 shows that beyond $\sim 8k_B T$ barriers, systems with all examined variations of driving forces (for no phase offset, $n = 3$ states) have reached the regime of simple exponential dependence on barrier height. Thus while the quantitative power-maximizing coupling may change somewhat with barrier height as it increases above $2 k_B T$ (already seen graphically in Fig. 3 in the main text), the qualitative findings are likely robust to such variation.

References

- (1) Risken, H. *Fokker-Planck Equation*, vol. 18 ed.; Springer, 1996; Chapter 11.3.
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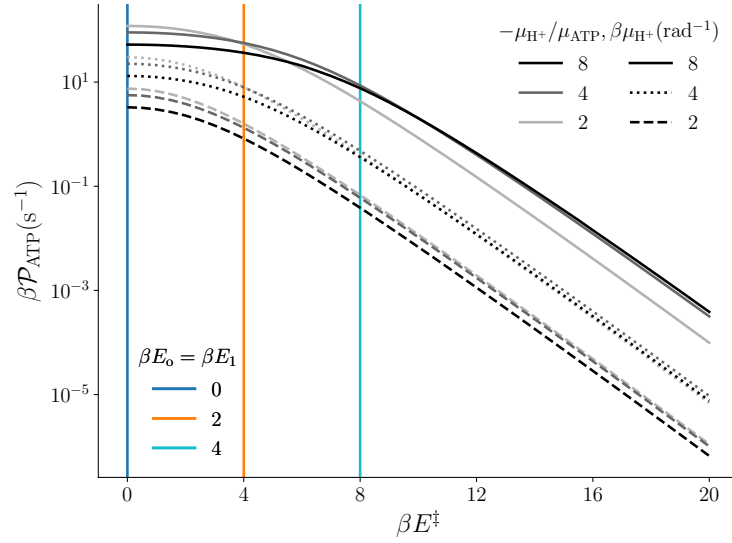


Figure S6: Output power as a function of barrier height $\beta E^\ddagger = \beta(E_o + E_1)$ for the tightly coupled system. Different greyscale shades represent different ratios $-\mu_{\text{H}^+}/\mu_{\text{ATP}}$ of driving forces (corresponding to the columns in Fig. 3 of the main text), and different linestyles represent different proton driving forces $\beta \mu_{\text{H}^+}$ (corresponding to the rows in Fig. 3 of the main text). Colored lines indicate barrier heights explored in the main text: $\beta E_o = \beta E_1 = 0$ (dark blue), 2 (orange), or 4 (light blue).