

COMMENTARY

Enhancing transport by shaping barriers

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Many molecular processes of great importance in both nature and technology speed up strongly if temperature is increased. Examples include chemical reactions, biomolecular rearrangements, the diffusion of atoms in solids, and the storage of information on magnetic recording media. In 1889, the Swedish physicist and chemist Svante Arrhenius was the first to give a physical explanation and mathematical description of this phenomenon in the form of the celebrated Arrhenius equation (1). Building on earlier work of the Dutch physical chemist Jacobus Henricus van 't Hoff, Arrhenius had realized that the particular form of the temperature dependence of reaction rate constants can be understood by assuming that the reaction from reactants to products involves passage through an activated state. As this activated state has a higher energy than the reactants, the reaction must cross an energy barrier and this happens only with assistance from thermal fluctuations of the environment. At higher temperatures, such fluctuations are more intense on average, making it easier for the system to overcome the barrier such that the reaction occurs with higher frequency. At low temperatures, on the other hand, thermal fluctuations of sufficient magnitude become rarer, leading to small reaction constants.

Today, 130 years after Arrhenius' brilliant insight, it is common textbook knowledge that many reactions can be viewed as the escape from a well in a potential or free-energy landscape over a barrier and that the resulting activation energy constitutes the central quantity determining the rate constant. In fact, reaction rates for activated processes depend exponentially on the activation energy and frequently vary by many orders of magnitude in response to changes in the temperature. What is often overlooked in textbooks, however, is that there are other factors besides the activation energy that significantly affect reaction rates and can be used to control them. This issue is addressed in Chupeau et al. (2), in which the authors show, using computer simulations and experiments, that the rate of escape from a well can be tuned by manipulating the shape of the barrier rather than its height. As demonstrated through

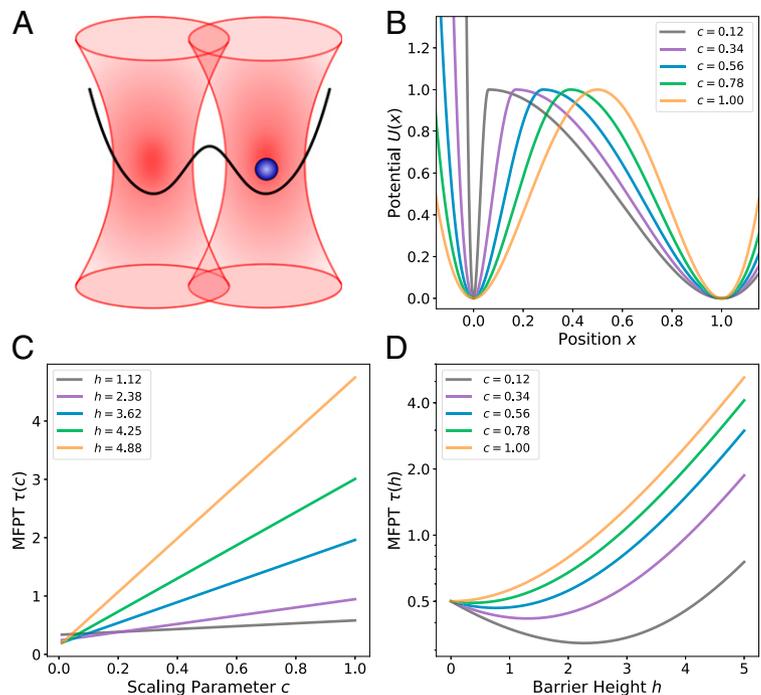


Fig. 1. (A) Schematic representation of a particle trapped in a bistable optical potential of two focused laser beams. The black line indicates the potential generated by the laser. (B) Various potentials with the same barrier height h and well distance but varying well width. These toy potentials, described in the main text, depend on a scaling parameter c that controls the relative position of the barrier and the width of the wells. (C) Mean first-passage time τ between the minima as a function of the scaling parameter c for various barrier heights h and overdamped dynamics. As small scaling parameters correspond to narrow initial wells, decreasing c reduces the escape time. (D) Mean first-passage time τ as a function of the barrier height for different scaling parameters c . For narrow initial wells (small c) increasing the barrier height initially reduces the mean first-passage time, which then goes through a minimum and eventually grows exponentially as expected by the Arrhenius formula for the transition rate.

their experiments (2), it is possible to enhance reaction rate constants by carefully engineering barrier profiles even while increasing the barrier height at the same time, thus contradicting the intuition informed by the Arrhenius equation only.

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In their paper, Chupeau et al. (2) first considered a simple two-well system evolving under the influence of friction and thermal noise as described by the Langevin equation. Importantly, the energies of the initial and final well are the same. Introducing their ideas in an overdamped setting, Chupeau et al. (2) optimized barrier profiles to yield the shortest mean first-passage time for directed transitions between the two wells, which is roughly the sum of the average time required to escape from the initial well and the typical time needed to slide down from the barrier to the bottom of the final well. The kinetics of escape from a potential well were investigated theoretically 80 years ago by the Dutch physicist Hendrik Kramers, who not only confirmed the dependence of the rate constant on the activation energy postulated by Arrhenius, but also explained how the escape rate depends on friction and on the width of the initial well and barrier (3, 4). More specifically, Kramers' theory predicts that the escape rate from the well is inversely proportional to its width, implying that one can enhance the escape rate by making the well narrow, effectively destabilizing it entropically. In addition, the time needed to slide down the barrier can be reduced by making the driving force toward the final well large, i.e., by making the barrier steep. The combination of these two effects can be exploited to make the rate of well-to-well transitions arbitrarily large, calling for the introduction of regularizing constraints into the analysis. By carrying out a variational analysis for two different regularizations, Chupeau et al. (2) derive general conditions for optimum barrier profiles under these constraints. They find that optimal profiles are efficiently approximated by N-shaped barriers. Remarkably, crafting potentials accordingly results in well-to-well transitions that are faster than free diffusion in the absence of the barrier.

The essential physics underlying this phenomenon are illustrated in Fig. 1 using a simple toy model, consisting of a particle moving in one dimension in a bistable potential of the form $U(x) = h\{1 - [2x/s(x)]^2\}^2$. Here h denotes the height of the barrier and $s(x)$ is a scaling function that controls the relative width of the left and right wells. Such a potential can, for instance, be viewed as arising from intensity gradients in laser beams (Fig. 1A). The scaling function chosen here is $s(x) = c\theta(-x) + (2-c)\theta(x)$, and hence the potential $U(x)$ depends on the parameter c . This particular parameterization ensures that the distance between minima remains constant, whereas their relative location with respect to the barrier maximum can be controlled. (Note that in Fig. 1A the potentials are shifted horizontally to make the positions of the minima coincide.) Decreasing the scaling parameter from $c = 1$ makes the left well narrower and the right well wider, entropically favoring the latter (Fig. 1B). The mean first-passage time for well-to-well transitions in our toy model is a linearly increasing function of the parameter c for fixed barrier height h (Fig. 1C); i.e., making the initial well narrower by decreasing c increases the escape rate from the well. Considering the mean first-passage time as a function of the barrier height h for fixed parameter c (Fig. 1D), one finds that its quantitative behavior is dominated by exponential growth for larger barriers, but exhibits a minimum for sufficiently narrow starting wells (for the given potential this occurs whenever $c < 1$ holds). Hence, in some cases making the barrier higher indeed speeds up the transition on average.

To verify the results of their theoretical analysis, Chupeau et al. (2) carried out experiments using an ingenious combination of microfluidics and optical tweezers (5). Optical forces induced by intensity gradients in strongly focused laser beams can be utilized

to manipulate matter at the nanoscale with spectacular accuracy, as evidenced by many applications in the physical sciences and biology (6, 7). For instance, experiments based on optical trapping have been used to verify fluctuation theorems that illuminate the nature of the second law at the nanoscale (8–10) and to confirm the so-called Kramers turnover for the friction dependence of the escape rate from a metastable well (11, 12). In their work, Chupeau et al. (2) tested their theoretically predicted speed-ups by means of

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a colloidal particle confined to a narrow microfluidic channel and exposed to a potential landscape created by a holographic optical tweezer. Without laser forces, the particle moves diffusively along the axis of the channel with constant diffusivity. When the laser potential is turned on, however, a substantial increase of the translocation rate of the colloidal particle occurs. The potential is tailored to be roughly N-shaped, as suggested by the optimization procedure, and the potential at the initial and the final point is the same so that no net driving force acts on the colloidal particle. Nevertheless, a speed-up factor of about 2 is obtained compared to free diffusion, conforming with theoretical predictions.

While the experiments of Chupeau et al. (2) were carried out in the overdamped regime in which friction dominates, theoretical considerations supported by computer simulations indicate that profile-induced speed-ups persist also for lower frictions. In this underdamped regime, however, inertial effects reduce the achievable speed-up factors and in the limit of vanishing friction the external potential ceases to enhance the escape rate. Experimentally, the effect of barrier profiles on the escape rate may be probed using laser-trapped levitated nanoparticles, which have been successfully used to study friction and noise-dependent phenomena like stochastic resonance (13) or the rotation of nanoparticles driven by circularly polarized light (14). In such levitodynamical setups, the damping is controlled by the gas pressure in a vacuum chamber, making it possible to tune the friction coefficient by several orders of magnitude.

The work of Chupeau et al. (2) is also relevant for the question of whether and how potential shaping is exploited in biological systems to enhance the rates for molecular translocation through nanopores. Recent theoretical studies (15, 16) indicate that the strength and spatial distribution of molecule/nanopore-channel interactions affect the translocation kinetics. In particular, binding sites located close to the pore exits appear most effective in maximizing molecular currents, reminiscent of the N-shaped potentials discussed by Chupeau et al. (2). Another way to change the dynamics of escape from a potential well is to introduce persistent motion as it occurs in active matter consisting of self-propelling particles (17, 18). In the future, it will be interesting to explore the interplay of such activity with the barrier shaping examined in the important work of Chupeau et al. (2).

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