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Optimally controlled optomechanical work cycle for a molecular locomotive

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Abstract

This work seeks to apply the laser optimal control technique to light-driven molecular motors. Taking a recently proposed molecular locomotive as a model system, a control loop is developed specifically for it, and concrete schemes for experimentally closing the loop are devised. A list of unique control objectives is rigorously formulated from the nanomachinery perspective, and corresponding optimization is made feasible by an innovative application of the established technique of closed-loop learning control. The optimization may be pursued for individual laser operational steps as well as for the overall nanolocomotion performance of the entire work cycle. The locomotive optimal control, capable of co-adapting the laser procedure and the periodically driven molecular dynamics, essentially leads to an optimally performing optomechanical work cycle for the locomotive beyond any model-based pre-designed version. These findings reveal a great potential of laser optimally controlled nanowork cycles in the emerging field of nanomachinery.

(Some figures in this article are in colour only in the electronic version)

1. Overview

1.1. Work cycles for molecular motors

In a famous talk in 1959, the physicist Feynman called the scientific community to the challenging task of making functional devices even down to the submicroscopic scale [1]. Of particular interest is his enquiry into the possibility of making 'small but movable machines' (in his words). He encouraged: 'consider any machine—for example, an automobile—and ask about the problems of making an infinitesimal machine like it'. Over the past decades the fields of nanoscience and nanotechnology have made steady progress towards the goal of making movable nanomachines. Especially remarkable is the growing list of artificial molecular motors realized in the laboratory. These experimental attempts are largely inspired by

biological motors, as their subtle molecular mechanisms start to be revealed by single-molecule studies [2, 3]. The man-made motors are mostly made of exotic synthetic molecules [4–10] or biomolecules such as DNA [11–14], and are capable of controlled intramolecular rotation or translocation when stimulated by light or chemical fuels. The accomplishments in artificial molecular motors, though still by far no match to biological motors, are fascinating, and are leading us towards a new field of molecular machinery.

As an analogue to a conventional heat engine whose continuous functioning relies on its work cycle, a nanomachine such as a molecular motor must have a nanoscale work cycle, which is a properly regulated sequence of molecular events such as energy injection, conversion and mechanical rectification, etc. When the set of molecular events is repeated cyclically, the motor moves processively. In his talk, Feynman pointed out that the conventional Carnot-type work cycles driven by a temperature difference are impossible for a submicroscopic machine, because heat transfer quickly demolishes any temperature gradient over such small distances. He argued that 'this rapid heat loss would prevent the gasoline from exploding, so an internal combustion engine is impossible. Other chemical reactions, liberating energy when cold, can be used. Probably an external supply of electrical power would be most convenient for such small machines' [1].

The importance of establishing general mechanisms for machine work cycles was probably first pointed out by Carnot. In his historic monograph *Reflections on the Motive Power of Fire, and on Machines Fitted to Develop that Power*, he wrote: 'It is necessary to establish principles applicable not only to steam engines but to all imaginable heat-engines, whatever the working substance and whatever the method by which it is operated' [15]. The Carnot cycle and related theory are seminal in the later establishment of the second law of thermodynamics. While it is concluded that the Carnot cycle loses validity for isothermal nanomotors, the general and sufficient guidelines for implementing nanowork cycles have yet to be developed. To achieve a directed rotation or translation at the nanometre scale, a molecular motor must pay an energy price to overcome the detailed balance that is a consequence of the second law of thermodynamics. More importantly, the energy price must be paid in a proper way, because the directional nanoscale movement otherwise would be readily overwhelmed by thermal and quantum fluctuations of the motor system and its environment.

Various mechanisms for molecular motors have been proposed, with some having properly biased thermal fluctuations as a major element of the desired nanomotion [16–23], and others placing more emphasis on deterministic, ballistic movement such as decisive power strokes [2, 24–27]. A prominent example of the former category is the Brownian motor mechanism that has turned out to be rather successful in understanding a broad range of biological and artificial systems [17–23]. However, the Brownian motor theory, among many other molecular motor theories, is mostly aimed at establishing a rectification mechanism for directional motion at the nanoscale. Largely missing are molecular physics mechanisms that substantiate or/and implement the various proposals of motional rectification. This is particularly the case when nanoscale track-walking is concerned. For example, it is not clear how to concretely deploy the Brownian motor mechanism into a real molecular system to achieve a hand-over-hand track-walker like biomotor kinesin [16, 28, 29]. Therefore, physically sound and practically workable molecular physics mechanisms for nanowork cycles should be among the list of pursuits for the field of nanomachinery in the future.

1.2. Laser-driven molecular work cycles

Laser driving of molecular motors possesses some unique merits as compared to other means. While a chemically pumped motor generally requires a liquid environment due to diffusive

supply of molecular fuels, light driving has the advantage of delivering energy to a motor from a distance, thus allowing for motor operation in a variety of environments. Absorption of a photon in the visible or ultraviolet spectrum instantaneously injects a few electron volts of energy into the motor system. Such an amount of energy is much larger than that released by an event of ATP hydrolysis. Therefore a laser powered motor has the potential of generating a pulling force much larger than those of ATP fuelled biomotors. Furthermore, for molecular motors, and nanomachines in general, lasers may play a larger role than merely serving as energy source. Ultrashort laser pulses capable of coherently manipulating molecular dynamics also provide a powerful technical means for operating a molecular motor [30].

Laser-driven molecular optomechanical work cycles have a solid molecular physics foundation. In fact, numerous molecular optomechanical devices have been successfully fabricated over the last decade; these are mostly based on molecular photoisomerization as a common mechanism for energy injection or ultrafast switch. A recent experiment by Hugel *et al* [31] nicely demonstrated an optomechanical energy conversion cycle at single-molecule level. They fixed a synthetic polymer molecule between an AFM tip and a substrate by covalently connecting both ends of the molecule with the tip and substrate respectively. By shining a laser to the photoisomerizable molecule and adjusting the height of the tip according to molecular length change, they created a single-molecule work cycle by which light energy was periodically converted into mechanical work.

Laser-driven molecular motors have long since been sought theoretically as well as experimentally. While a variety of theoretical designs have been proposed [25, 30, 32, 33], experimental demonstrations have been successful mostly for molecular rotors [7, 9] and molecular shuttles based on exotic synthetic molecules [5, 8]. Inspired by the experiment of Hugel *et al* [31], I have recently proposed a laser-operated molecular locomotive [30], which, made of an easily available photoisomerizable polymer chain, is able to directionally climb a linear track wherever the track reaches. The core mechanism for the nanolocomotion is a multistep molecular optomechanical work cycle, in which molecular photoisomerization drives decisive power strokes. The molecular locomotive is unique in that the entire procedure for its operation can be executed by lasers.

1.3. Optimal laser control of molecular motors

Not only are lasers able to execute a nanowork cycle. It is also possible to best adapt the laser procedure up to an optimal performance of the work cycle. The technological ground for laser operation optimization for nanomotors already exists, which is the well-established field of laser coherence control [34]. Thanks to breakthroughs such as the achievement of fast, programmable shaping of ultrashort pulses and the introduction of the closed-loop learning control method, optimal laser operations have been experimentally demonstrated for a growing list of molecular processes, such as selective electronic excitation [35], breaking and rearrangement of chemical bonds in polyatomic molecules [36–42], and intermolecular energy transfer [43]. These achievements open the possibility of operational optimization for light-driven molecular motors.

The basic idea of laser coherence control is to tailor exciting radiation to generate selective quantum molecular dynamics with such interferences that the manifold of the final molecular states has a population distribution satisfactorily close to the pre-designated output [44, 45]. Laboratory control of molecular dynamics has been made feasible by ultrashort laser pulses capable of depositing energy into selected motional modes at a pace faster than intramolecular vibrational relaxation (IVR). However, the task of theoretically designing the optimal control field, i.e. electric field $\boldsymbol{E}(t)$ of the laser pulse for a control objective, has been hindered by

the extreme difficulty in solving time-dependent Schrödinger equations for real molecular systems [46]. The difficulty of control field design has been successfully circumvented by the introduction of the self-learning laser control technique [35, 47], in which pattern recognition algorithms analyse outputs of control experiments round after round to identify the attractive features of the laser field. Combining the computer-controlled pulse-shaping technique with the use of noise-resistant genetic or evolutionary algorithms for pulse assessment, the so-called closed-loop learning control procedure [48] may be started with any trial pulses to automatically draw the molecular system towards the desired control objective. Such a model-free, self-starting capacity has turned out to be the key for bringing a broad range of molecular systems under successful laser control [48]. It will be interesting to see if the success of optimal laser control will be able to extend to molecular motors.

There generally exists much room for optimization of laser operations for light-driven molecular motors. The laser procedure originally designed for running the molecular locomotive is rudimentary in the sense that there is no consideration of optimality. A similar situation exists for other laser-operated nanosystems too. Extension of the powerful laser control technique to molecular motors will lead to the topic of optimal control of nanomachinery. We thus shall seek a novel role of lasers for nanomotors, which is a means of control in addition to an energy source and an operational tool. In the present contribution I shall focus on the molecular locomotive, and develop optimal control for its optomechanical work cycle. Unique control objectives for the purpose of a successful nanolocomotion will be formulated, which are innovative ideas, yet within reach of the established optimal control technique. I shall first seek to optimize the effectiveness of individual laser operations for major steps of the work cycle. Then I shall seek to improve the overall nanolocomotion performance by introducing system-level optimizations which involve the entire set of laser operations for a full work cycle. A control loop will be developed specifically for the molecular locomotive to facilitate its optimization, and concrete schemes for experimentally closing the loop will be presented. I shall show that a closed-loop learning control procedure for the locomotive is able to close in on the right laser operations for an optimal functioning of the work cycle, despite a great number of uncertainties on details of the laser-driven molecular dynamics of the locomotive–track in a solution environment.

The paper is organized as follows. In section 2, I shall briefly review the major elements of the optomechanical work cycle for the locomotive with some new thoughts added on the choice of molecular systems for laboratory implementation. In section 3, I shall address optimal control of several key operational steps of the work cycle. Detailed physical models for these operations will be presented, and optimal control schemes will be designed based on the physical models. In section 4, I shall introduce the concept of an overall optimal control for the entire work cycle. The relevant control objectives will be formulated, and laboratory schemes developed. In section 5, I shall draw conclusions.

2. Optomechanical work cycle for a molecular locomotive

The molecular locomotive is a single, synthetic polymer chain that stretches or contracts itself sizably when illuminated by lasers of different colours. As demonstrated by the experiment of Hugel *et al* [31], such a photoisomerizable polymer can serve as a single-molecule optomechanical engine. The extending or contracting of the polymer chain closely resembles thrusts of a piston in a macroscopic combustion engine. Nevertheless, such a molecular engine, when freely floating in solution, is unlikely to do anything meaningful by its random mechanical thrusts. However, when it is restricted between a solid surface and a deflectable AFM tip, as in the experimental setting of Hugel *et al* [31], the engine may

cyclically convert light energy into mechanical work by properly coordinating light colours with the tip adjustment. The single-molecule optomechanical engine may drive a directed nanolocomotion when placed in another restricting setting formed by a linear track, and when the restrictions by means of engine–track interaction are properly modulated. Thus, aligning the molecular engine on the track, and with two 'head groups' at both ends of the engine polymer being principally responsible for the engine–track interaction, we essentially have all of the physical constituents for a molecular locomotive. Further gaining control over the locomotive–track interaction in addition to photoisomerization, particularly control of binding and unbinding of the head groups with the track, we have the necessary means to run the locomotive along its track. Finally, and most importantly, a carefully formulated work cycle, which coordinates laser-driven mechanical thrusts of the locomotive with the regulation of the locomotive–track interaction by yet more lasers, will enable the locomotive to climb the molecular track step after step into a chosen direction, much like an inching nanoworm.

The optomechanical work cycle for the molecular locomotive is schematically illustrated in figure 1. Suppose the locomotive is initially in the contracted state with front and rear heads both docked to the track. Laser undocking of the front head is followed by laser-driven stretching of the locomotive. Either as a naturally occurring process or being assisted by a laser, docking of the forward-moving head at a new binding site anchors the extended locomotive to the track. Then the rear head is undocked, and the locomotive is shortened to pull itself ahead. Docking of the trailing head resumes the initial state of the locomotive, but it now sits one binding site forward. The whole series of six laser operations for one full step can be repeated to drive a continuous nanolocomotion. The inchworm gait for nanolocomotion requires rather delicate locomotive–track interactions and their fine-tuning by the work cycle.

An attractive feature of the locomotive work cycle is that a direction for the nanolocomotion may be chosen by timing laser pulses of different colours. The directionality comes from the spectrally distinct laser pulses for modulating the two head groups' interaction with the track. This spectral requirement may be met by use of two different head groups and the track is not necessarily polar. The track should contain a series of equally spaced 'harbouring groups' to host the interaction with the head groups; thus the spatial period of the harbouring groups should reasonably match the length difference between the fully extended and fully contracted configurations of the locomotive chain. The head–harbour interaction may be either physical or chemical in nature. A chemical bonding is preferred for several reasons. First, this ensures a robust locomotion against strong fluctuations. Second, holding the 'ground' firmly is also necessary for the generation of a large pulling force. Third, and most importantly, a chemical bond between the head and harbour, with its binding energy over one order of magnitude larger than those of physical contacts typically occurring in the locomotive–track interface, readily makes itself the sole superior player, providing a unique handle for laser regulation of the locomotive–track interaction. Therefore, synthetic linear structures, for example nano- or micro-tubes, which inherently possess or are able to accommodate chemically tethered harbouring groups, may be good candidates for the track. Laser driving inevitably produces a large amount of heat within the locomotive because only a portion of the photon energy is eventually converted to mechanical work. Therefore, the ability of quickly diverting heat from the locomotive is another criterion for choosing the track. In this regard carbon nanotubes may be a good choice due to their superior thermal conductivity [49]. Properly engineered biological microtubules may be a choice for the locomotive track too, if they are compatible with the chemical bonding between the locomotive heads and the track. Otherwise, a physical mechanism for the head–harbour binding has to be developed. One such example is laser-controlled hydrogen bonding used in a molecular shuttle [8].

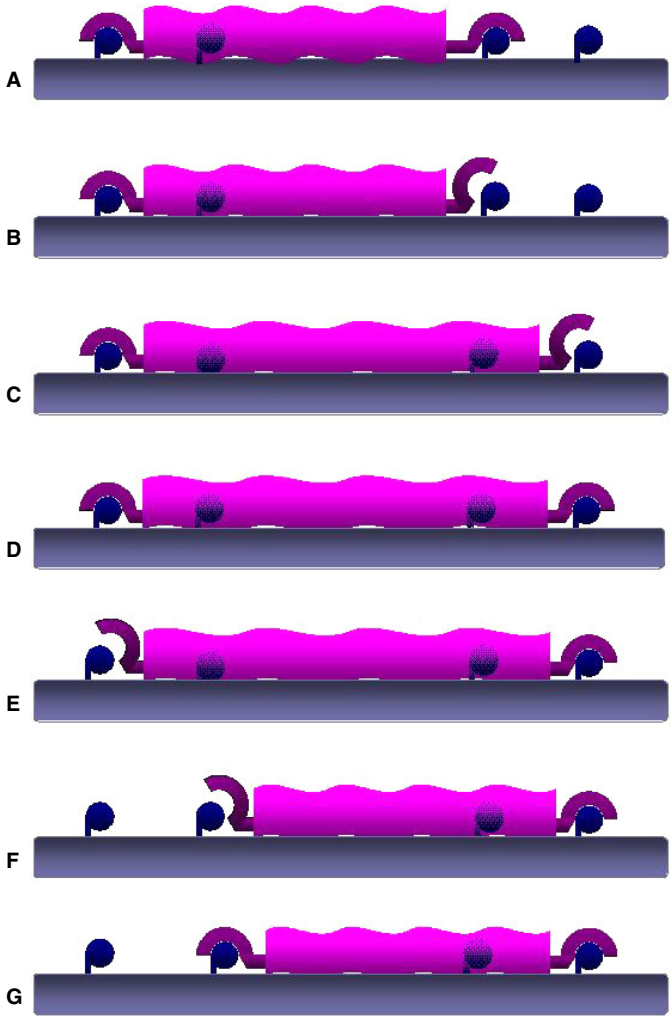

Figure 1. Illustration of the optomechanical work cycle for the molecular locomotive. The locomotive is initially in the contracted state with front and rear heads both docked to the track. Laser undocking of the front head is followed by laser-driven stretching of the locomotive. Either as a naturally occurring process or being assisted by a laser, docking of the forward-moving head at a new binding site anchors the extended locomotive to the track. These operations, illustrated by pictures (B)–(D), accomplish one half of the work cycle. Then the rear head is undocked, and the locomotive is shortened to pull itself ahead. Docking of the trailing head resumes the initial state of the locomotive, but it now sits one binding site forward. Thus, the operations shown by pictures (E)–(G) finish another half of the work cycle. The whole series of operations for one full step can be repeated to drive a continuous nanolocomotion. Please note that the locomotive cannot actually site on the track as 'comfortably' as the pictures make it appear—both the locomotive and the track keep fluctuating randomly against each other in the real molecular world.

3. Optimal control for key steps of the locomotive work cycle

To accomplish a whole work cycle, three types of laser procedure are necessary, which are laser driving of the locomotive isomerization, laser undocking of a head group from the track, and the reverse laser docking of the head to the track. For an appropriate choice of physical

constituents of the locomotive–track and the solution environment, and with laser sources of certain power output, the effectiveness of the three laser operations may be readily improved by application of the optimal control technique. In this section I seek to optimize each of the laser operations with the control objective of maximizing the operational effectiveness, which can be quantified by the total probability of success over a fixed period of operation time.

In applying the optimal control technique to the locomotive work cycle, some unique challenges arise from the nanomachinery perspective. First, a locomotive strongly interacting with its track and the surrounding solution presents a problem of laser control of a single polyatomic molecule in a complex condensed matter environment. Second, the locomotive–track system is highly dynamic, because the work cycles periodically drive the system away from equilibrium. Furthermore, the large amount of heat produced within the locomotive–track system during each work cycle causes strong thermal fluctuations. The laser control must be able to cope with the locomotion dynamics and the cyclically energized fluctuations. While meeting these requirements is within reach of the established capacity of the laser control technique, innovative approaches are necessary. Because of great uncertainty about the optomechanics and thermodynamics of the locomotive through the laser-driven work cycle, the model-free closed-loop learning control best serves the purpose of optimizing the locomotive operations. In the following I develop control schemes for each of the laser operations on the basis of their physical mechanisms.

3.1. Locomotive isomerization

For the sake of an in-depth study we focus on poly-azobenzene as a specific candidate for the main body of the locomotive. The optomechanical capacity of such a polymer has been experimentally tested at single-molecule level [31], suggesting that it meets well the requirements for the locomotive [30]. In fact there exist many synthetic polymers suitable for making the locomotive, and we note that the control schemes developed here are applicable to other locomotive candidates too.

A convenient mechanism for isomerization of the locomotive is to drive its multiple isomeric units using visible or UV light. In such a photoisomerization process, a unit is first electronically excited from the ground state S_0 to the excited state S_1 or S_2, and then an internal conversion (IC) process quickly brings the unit back to the ground state through the conical intersection. After IC the unit usually has almost equal probability to go into either the *cis* or *trans* configuration [50, 51]. Therefore, several photons will be absorbed by a unit to guarantee its transformation into a target isomeric state. During each excitation–IC cycle, extensive intramolecular vibrational relaxation (IVR) occurs, leading to an internally hot unit up to 1000 K typically within picoseconds after the photon absorption. Because of the quantum nature of light absorption, individual units of the locomotive isomerize randomly. As a consequence, the process of saturating the entire locomotive chain into the target configuration will be accompanied by stochastic temperature hiking of individual units together with vigorous heat flow between them and into the track and environment.

The amplified thermal fluctuations may affect the laser–locomotive interaction. For example, large off-resonance may be caused and absorption efficiency reduced. Therefore, it is very desirable to work out a laser procedure that is able to cope with these strong fluctuations to robustly maintain a maximum rate for saturated isomerization of the whole locomotive chain. This task is intrinsically suited for the closed-loop control procedure, because the involved physical processes are reciprocally interdependent, i.e. the heating of the locomotive units, while being caused by the laser driving, influences in turn the driving efficiency. A learning control procedure, capable of automatically recognizing the interdependence patterns, will lead to an optimal laser procedure for locomotive isomerization.

Nanoscale heat generation and migration is by itself an important topic, particularly when occurring in functional molecular devices such as the locomotive. The capability of the learning control technique to reveal the complicated mechanism behind a successful control [48, 52] may provide much needed insights into the unique thermodynamics of the locomotive. Interestingly, Feynman argued in his famous speech that a really tiny machine 'will not run hot because the heat escapes away from such a small device very, very rapidly' [1]. A series of state-of-art studies provides growing evidence that nanoscale heat transfer depends sensitively on molecular details, much more subtly than suggested by a simple extrapolation of the classical heat conduction theory for bulk materials [53]. The issue of heating and cooling of the molecular locomotive had been addressed rudimentarily in our previous study [30], based on the classical theory of heat diffusion. A recent study in terms of detailed molecular mechanisms with major parameters deduced from experimental data predicts that an excited locomotive unit can cool down to the room temperature within 100 ps in water [54].

Even for small organic molecules such as azobenzene, the photoisomerization pathway remains a topic of debate [55, 56]. High-lying electronic excited states above S_1 and S_2 may be involved too, depending on the excitation frequency [57]. These excitation schemes require higher laser frequencies than those of the conventional excitation schemes discussed above, thus providing more spectral options for the laser operation of the locomotive isomerization. An optimal control procedure needs be separately applied to the various excitation schemes, because they lead to distinct different thermodynamics due to different photon energies.

3.2. Undocking and docking

In fact, selective cleavage and formation of chemical bonds occur naturally in many biological processes under sophisticated biochemical regulations. Associating and dissociating a molecular part from a host are also key operational steps in many functional molecular devices. For example, a recently developed bipedal molecular walker made of DNA molecules accomplishes leg-track association and dissociation via special chemicals, which have to be administered at each step from outside after the waste from the preceding step is washed away [14]. For the molecular locomotive being studied here, lasers are responsible for the task of attachment and detachment. A self-contained mechanism can be developed for the docking–undocking of the locomotive heads.

The self-containedness is ensured by introducing a pair of covalently bonded docking units into a head group of the locomotive, and also a pair of covalently bonded harbouring units into the harbouring group of the track. It is further required that both docking units are also chemically bonded with their host head while only one of the harbouring units is directly bonded to the track. How a head of the locomotive can dock to and undock from the track is illustrated in figure 2.[1] Once the couple of docking units of the head flies by Brownian motion close enough to the couple of harbouring units sitting on the track, thermal energy or additional energy supplied by lasers readily drives a switching of the two chemical bonds, thereby interlocking the locomotive and the track. This process occurs in a manner similar to a normal bimolecular reaction if both the docking units and the harbouring units are viewed as quasi-diatomic molecules. Thus, we have a diffusion-controlled, thermally assisted or laser-assisted docking. If the pair of newly formed bonds are kept sufficiently close to each other, reversing the above operations leads to undocking. Specifically, a laser breaks the interlocking chemical bond to engage the nearby bond of the head. A reverse bond switching then occurs and sets the head free. This is laser powered, sterically reinforced undocking.

[1] The figure depicts a twin-pulsed docking–undocking mechanism to be developed later in the section. Nevertheless, the figure also serves well a general discussion of docking–undocking operations.

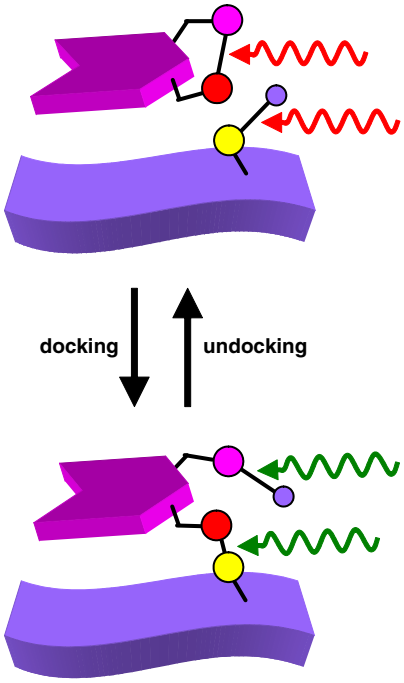

Figure 2. Illustration of a twin-pulsed scheme for docking and undocking of a locomotive head at a binding site of the track. Once a pair of docking units of the head diffuses close enough to a harbouring pair sitting in the binding site of the track, a couple of optimally correlated laser pulses readily co-drive a switching of the chemical bonds that eventually interlocks the locomotive and the track in a manner similar to a bimolecular chemical reaction. Another twin pulse coordinately injects energy into the interlocking chemical bond and the nearby bond of the locomotive head, leading to a reverse bond switching to set the head free.

The simplest procedure for head undocking can be the photodissociation of a single bond; molecular manipulation of this kind has already been achieved in learning control experiments. Two established experimental schemes may be adopted for the purpose of optimizing the undocking effectiveness. One is electronic excitation driven by high-intensity, femtosecond laser pulses in the near-infrared (IR) spectral range [36–38]. The strong radiation field forces the molecular vibronic levels into resonance through a combination of Stark shifting and multiphoton absorption, thus effectively removing the pulse bandwidth restriction on resonant excitation [36]. When integrated into a closed-loop learning control setup, this technique has demonstrated the capability of selective cleavage and rearrangement of chemical bonds in polyatomic molecules with dissociation energies up to 4 eV [36]. The other experimental scheme suitable for the undocking operation is vibrational ladder climbing (VLC) within the electronic ground state driven by mid-IR femtosecond pulses. With frequency chirped pulses [39, 40] or by the mechanism of infrared multiphoton excitation (IRMPE) [41, 42], this technique is able to excite successive levels in an anharmonic potential. Ground-state dissociation of polyatomic molecules has been successfully achieved within a timescale competitive even to that of IVR [42]. As compared to the first scheme of strong-field near-IR control, the mid-IR VLC procedure for head undocking does not directly involve electronic excitation. Therefore, the VLC undocking scheme may better avoid erroneous electronic effects, e.g. irreversible ionization.

The docking operation is much subtler than undocking. Ideally, head docking may occur automatically if the thermal energy is already sufficient to activate the quasi-bimolecular reaction. Nevertheless, we prefer developing a laser docking mechanism for the more general case of insufficient thermal activation. We proposed selective vibrational excitation of the docking and harbouring units as an effective mechanism to drive the bond switch for docking. The vibrational modes to be excited should be so chosen that they have a reasonably large component of motion along the reaction coordinate for the quasi-bimolecular docking reaction. Exciting the vibrational modes with mid-IR lasers will then effectively channel energy into the reaction pathway to accomplish the docking. This docking mechanism is technically feasible, since control of bimolecular chemical reactions by laser excitation of selected vibrations has already been successfully achieved in the laboratory [58, 59]. For the purpose of locomotive docking, simultaneous excitation of both the docking and harbouring units by twin pulses is preferred, because less energy then is required to be injected into either bond, reducing the possibility of bond dissociation prior to docking. The scheme of mid-IR driven VLC can be readily adopted for twin-pulsed docking.

This twin-pulsed docking mechanism, as illustrated in figure 2, does not struggle to accumulate a single high excitation against formidable IVR. Rather, two separate excitations, each of modest energy, are prepared. The key is to couple both excitations at the head–harbour encounter so that the two pieces of excitation energy are combined and efficiently channelled into the reaction pathway. The optimal shapes of the two simultaneously applied pulses may be worked out by a closed-loop laboratory learning procedure that naturally takes into account the interaction between the reactive partners. The resultant pulses will have a maximum effect when the reactants fall within the interaction range with each other. When they are far separated, neither will be affected much. Therefore, the learning control procedure is a fairly ideal solution to the task of laser-assisted docking between moving partners.

Apparently, the twin-pulsed mechanism and the related optimal control scheme can be conveniently used for the undocking operation too. This will lead to a solution much better than those offered by the single-pulsed undocking schemes discussed previously. Thus, the twin-pulsed mechanism provides a common basis for optimal control of both docking and undocking of the locomotive heads (see figure 2).

3.3. Experimental implementation

For the optimal control of individual laser operational steps for the locomotive work cycle, the established technique of closed-loop learning control may be used rather straightforwardly. The processes of photoisomerization, and breaking and switching of chemical bonds fall within the regime of quantum control, in which the major control variable is the pulse shape of the laser field applied. Experimentally, an ultrashort laser pulse is shaped by adjusting the phase and amplitude of each frequency component of the pulse. Such a pulse-shaping procedure can be performed in the laboratory automatically under computer control.

The output of an applied control must be measured in order to feed the data back into the control loop. To obtain sufficient signals the measurement should be performed on an ensemble of a large number of synthetic locomotive–track systems. The observable is the percentage of successful events after applying an operation over a certain period of time. For measurement of isomerization effectiveness, conventional spectroscopic techniques are sufficient to detect population change in the locomotive isomeric states. For docking–undocking measurement, a technical means capable of resolving the head–harbour distance up to nanometre precision is required. A convenient choice for this purpose is the well-developed technique of fluorescence resonance energy transfer (FRET) [60]. FRET is a distance-sensitive non-radiative migration

of excitation energy from a dye molecule (donor) to another nearby dye molecule (acceptor). Monitoring fluorescence emissions from the acceptor under selective laser excitation of the donor will yield information on the separation between the dye pair. The FRET technique is able to resolve distances from a few nanometres up to 10 nm, and is therefore suited for the purpose of identifying docking and undocking events. It is a routine laboratory job to label an appropriately chosen FRET pair site-specifically to locomotive heads and track harbours. Docking and undocking experiments can then be performed on an ensemble of thus prepared locomotive–track samples, providing effectiveness data for assessment of the control fields applied.

4. System-level optimization of the locomotive work cycle

To complete a work cycle for the locomotive six laser operations are required, and the pulses must be arranged in a proper temporal sequence. The overall nanolocomotion performance depends not only on the effectiveness of individual laser operations, but also on time matching between them. Therefore, improvement of the locomotion performance is largely beyond the reach of the optimal controls designed in the preceding section for single operational steps. Rather, an optimal nanolocomotion can be sought by collectively optimizing the whole set of laser operations for a full work cycle. Such a system-level optimization essentially derives from the machine perspective of the molecular locomotive, and provides a unique laser optimal control problem.

In this section I shall construct system-level optimal laser controls of the locomotive for two specific control objectives, namely maximum speed and optimal robustness of the nanolocomotion. Both control objectives will be rigorously formulated, and the control outcomes unambiguously quantified. I shall also elaborate an experimental scheme that allows a convenient measurement of the control outputs for feedback into the locomotive control loop.

4.1. Control objective 1: maximum speed

The locomotion speed is determined by the average time to run a full work cycle (τ_{cyc}), because each work cycle moves the locomotive over a certain distance that is set by the period of the binding sites in the track. Several time-consuming steps of the work cycle, especially locomotive isomerization and diffusive search of a head for a binding site, are major determinants for τ_{cyc}. Heat plays a role too by its influence on locomotive isomerization and head diffusion. These important processes, i.e. photoisomerization, intrachain diffusion, heating and cooling, are all stochastic in nature, and depend sensitively on the solution environment. Modelling alone can at best predict a far upper limit to their duration, and is unable to determine the optimal speed. A previous estimate of these timescales concluded that an average speed of 1 μm s^{-1} (corresponding to $\tau_{\mathrm{cyc}} \approx 8$ ms) may be achieved by existing technical means [30]. A closed-loop learning control procedure is able to fully exploit the capacity of the locomotive–track-environment for an optimal speed.

The optimal control for the objective of reaching a maximum locomotion speed may simply be carried out on the basis of the pre-optimized pulses for individual steps of the work cycle. Only temporal correlations between these steps, namely time delays between the multiple pulses, are adopted as control variables for the system-level optimization. Since the pulse delays are generally well beyond the typical lifetime of molecular coherence in solution, this type of system-level control is largely classical. In this case the model-free closed-loop learning control provides a valuable tool as well, because of its capacity to optimally adapt the laser procedure to the cyclically energized thermodynamics of the locomotive–track system.

The optimal pulse delays ensuring a maximum locomotion speed can be readily worked out despite great uncertainties about such key steps as locomotive cooling and head search for binding.

To form the control loop in the laboratory, measurement of locomotion speed achieved by a control field must be performed. This can be done using an ensemble of synthesized locomotive–track systems with FRET labels, but the deduction of speed information needs some innovative approaches. We propose a labelling scheme in which every binding site of the track contains the same donor species, and two different acceptor species respectively sit in the leading and trailing heads of the locomotive. As the locomotive runs under the control field, the FRET signals of the acceptors will disappear and reappear periodically. These fluorescence periods are readily detected, yielding the values for τ_{cyc}. Thus, this experimental procedure is able to directly measure the locomotion speed, producing the necessary feedback to the control loop. More details of the experimental scheme are presented in figure 3 and the captions.

4.2. Control objective 2: optimal robustness

Locomotion robustness measures the capacity of the locomotive–track system to function properly in defiance of all the negative factor. The robustness may be quantified by locomotion processivity, namely a maximum number of consecutive steps regardless of its speed. The locomotive robustness thus defined reflects fatal loss of functionality of the machine system because of erroneous steps of the work cycle[2]. The whole locomotive chain may fall off its track due to mismatch between operational steps. It is also possible that the locomotive remains on the track but deadlocked in an unrecoverable misstep, for example a premature dissociation before the docking partners find each other. These fatal errors may occur by a non-trivial probability due to strong thermal and quantum fluctuations accompanying the nanolocomotion. Limited reproducibility of the operational laser pulses due to the laboratory instability of laser sources and pulse shapers also tests the robustness of the locomotive work cycle.

A self-adapted optimal control procedure is able to tailor the locomotive work cycle to better cope with all of these fluctuations for a maximum robustness. The number of consecutive steps, which quantifies the locomotion robustness, can be deduced from the temporal patterns of the fluorescence signals in the same experimental setting as for the speed control (see figure 3 and the captions). Optimal locomotion robustness may serve as an independent control objective, or the robustness may be optimized together with speed. In either type of robustness control, both pulse delays and pulse shapes for key operational steps must be taken as control variables, because fatal errors may occur either within individual steps or by misconnections between them. If the two classes of error are not correlated with each other, the refinement of pulse shapes and the adjustment of pulse timings will be largely uncoupled through the optimal control loop. However, when the pulse delays are close to being optimal, as may occur in a speed–robustness joint control procedure, individual erroneous steps may develop a correlation with step mismatch. Then the pulse shape fine-tuning and the timing adaptation will be coupled together by the control loop. The pulse shapes are key control variables in the closed-loop coherence control for individual steps, while the pulse delays serve as control variables largely in a classical sense. Thus, we will have a quantum-classical hybrid optimal

[2] In the robustness control we do not consider the phenomena of photo-bleaching and -blinking, in which any light-responding part of the locomotive–track loses absorption ability permanently or temporarily so as to terminate the locomotive function. The two processes are largely determined by inherent molecular properties. We assume that their occurrence is kept rare for a reasonably large number of locomotive steps by choice of molecular modules for the locomotive–track system.

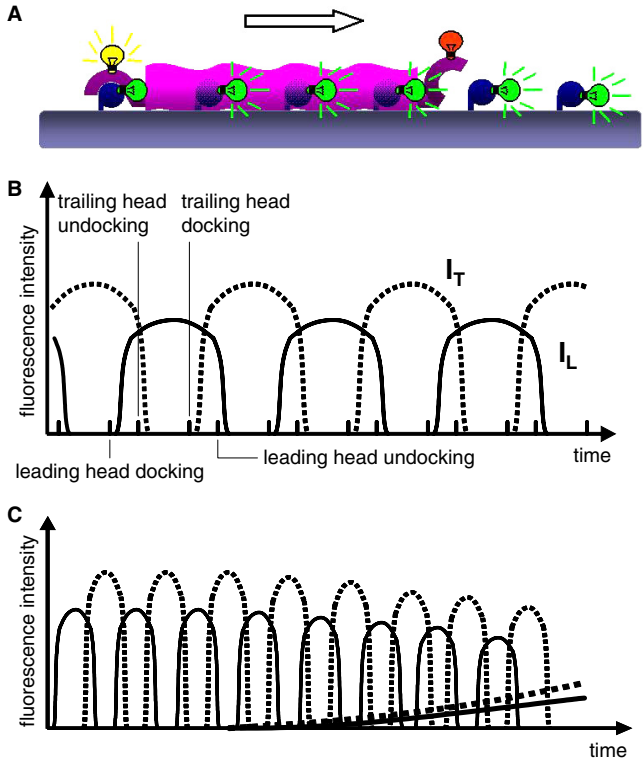

Figure 3. An experimental scheme to measure nanolocomotion performance for feedback into the control loop for the molecular locomotive. (A) The binding sites of the track are labelled with identical dyes which serve as energy donors, while two types of acceptor dyes are tethered to the leading and trailing heads of the locomotive. In a FRET measurement only the donors are selectively excited by lasers. The donor excitation energy may transfer to a nearby acceptor in a docked head (the trailing head in the depicted case), but is unlikely to transfer to any distant acceptor in an undocked head (the leading head shown in the figure). Consequently, the acceptor of a docked head emits fluorescence, but that of an undocked head does not. Ensemble measurement of a large number of labelled locomotive–track systems is able to yield average values for locomotion speed and consecutive running length. (B) Typical fluorescence spectra of the dyes in the leading (solid curves) and trailing (dotted curves) heads for an ideal locomotion through repeated work cycles in an ensemble measurement. The timing of major laser operational steps is indicated. The periodic patterns of the spectra directly yield average values of locomotion speed. (C) Typical fluorescence spectra measured for a long running time of the locomotives. Note that a locomotive that is erroneously stalled on the track will contribute a flattened spectrum over the observation time, while a locomotive falling away from the track does not emit at all. In both cases of dysfunction, the distinct periodic feature is lost. As dysfunction develops and the working population is reduced, the intensity for the periodic peaks decreases. Meanwhile, the accumulated dysfunctional population leads to a featureless background, which gradually increases with time. The decrease of the working population may be deduced from the spectra, yielding an average processive running length of the locomotive ensemble.

control, in which competition and compromise occur between system-level optimization and individual-step optimization.

For such an evolving technique as the laser-driven nanomachinery, robustness is an issue of paramount importance. Lack of robustness prohibits reliable measurement crucial to improvement of a system. As far as the molecular locomotive is concerned, one great challenge lies in how to make a first laboratory prototype system that possesses a minimal, yet workable

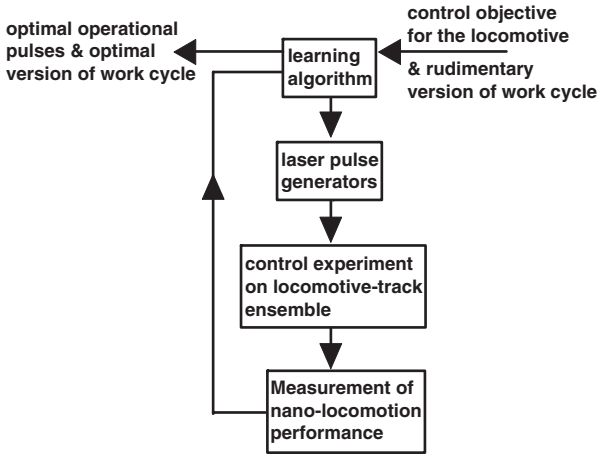

Figure 4. Illustration of the control loop for the molecular locomotive. The laser pulses and their time correlations are iteratively adapted to the periodic locomotion dynamics and to fluctuations of the entire locomotive–track-environment system. The output is not only an optimal set of laser operations for running the locomotive, but also a drastically improved version of the work cycle itself.

level of robustness. Once such a trial system is achieved, the proposed robustness control can be applied. The output laser procedure will drastically improve the system's robustness, which will in turn make possible control experiments towards yet more objectives. By their self-adapting capacity these closed-loop learning control experiments will serve as invaluable guidance for developing new generations of prototype systems for the molecular locomotive.

5. Conclusions and perspective

I have shown that there is big room for optimizing the laser operations for a proposed molecular locomotive, and the optimization can indeed be done by an innovative application of the established closed-loop laser learning control technique. The feasibility of the locomotive optimal control is substantiated by a concrete control loop that has been developed specifically for the nanomotor through the above sections. Measurement schemes have been established for unique observables quantifying the nanolocomotion to experimentally close the locomotive control loop. As illustrated in figure 4, the control loop for the molecular locomotive consists of (1) a control objective uniquely defined for the locomotive, (2) genetic algorithms for control field assessment according to the control objective and the feedback of control outputs, (3) control fields generated under guidance of the evolutionary algorithm, (4) physical observables quantifying the control outputs, and (5) experimental schemes to measure the control outputs for feedback into the control loop. The locomotive control loop is iteratively cycled by a self-learning procedure to close in on the right laser operations for an optimal nanolocomotion in a model-free manner.

The optimal control of the locomotive may be performed for individual laser operational steps of the work cycle, as well as on the system level for the entire work cycle. The effectiveness of photoisomerization of the locomotive, and laser docking and undocking between a locomotive head and the track, may be drastically improved by the optimal control procedure. More importantly, the locomotion speed and robustness, which characterize the performance of the locomotive–track as a whole machine system, may be optimized too.

The work cycle of the locomotive is characteristic of a strong coupling of laser-driven molecular optomechanics and periodically energized thermodynamics. The closed-loop learning control may start with a minimum knowledge of the complex molecular dynamics, and coevolve the laser procedure and the system dynamics towards an optimal working of the work cycle. The laser means, serving essentially as a 'fleeting' component of the optomechanical work cycle, is further interwoven with physical capacity of the locomotive–track system through the optimal control procedure. The output work cycle is so drastically enhanced that it essentially represents a new version greatly beyond the original, pre-designed one. Moreover, the mechanism behind the quality improvement of the work cycle may be revealed by combining the optimal control experiments with molecular modelling of the nanolocomotion. Thus, the locomotive optimal control technique as outlined here will prove a powerful tool for future development of the nanomotor.

The nanolocomotive optimal control highlights the great potential of applying the well-established and ever-advancing technique of laser optimal control to the emerging field of nanomachinery. The marriage between the two fields as attempted in the present study, being convenient at first glance, reveals a great depth of scientific legitimacy and even inevitability. With a designated working function as the ultimate purpose, a genuine machine is intrinsically subject to control for unifying its many parts into a working entity, and optimization is always desirable to better achieve the target function. While extension of control concepts to nanoscale machines is an obvious necessity, the laser optimal control provides a suitable technical means. In fact, the optimized laser operations such as isomerization, docking and undocking, while being crucial to the molecular locomotive, may readily find applications in a wide variety of light-responding molecular devices and machines. More importantly, the control strategies established in the present study, particularly those aiming at a system-level optimization of the nanomotor performance, may be extended to other light-driven nanosystems. I anticipate a bright future for optimally laser-controlled nanomachinery.

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