MRS Communications

https://doi.org/10.1557/s43579-022-00211-7

MRS Communications

Early Career Materials Researcher Prospective

Switching the conductance of a single molecule: Lessons from molecular junctions

Haixin Zhang, and Mehrdad Shiri, Department of Physics and Astronomy, Mississippi State University, Mississippi State, MS 39762, USA
Ridwan Tobi Ayinla, Department of Chemistry, Mississippi State University, Mississippi State, MS 39762, USA
Zhe Qiang, School of Polymer Science and Engineering, University of Southern Mississippi, Hattiesburg, MS 39406, USA
Kun Wang, Department of Physics and Astronomy, Mississippi State University, Mississippi State, MS 39762, USA; Department of Chemistry, Mississippi State University, Mississippi State, MS 39762, USA

Address all correspondence to Kun Wang at **kw2504@msstate.edu**

(Received 15 May 2022; accepted 15 July 2022)

Abstract

The concept of using single molecules as functional building blocks in electronic circuitry represents the ultimate device miniaturization and has garnered tremendous attention from physics, chemistry, and engineering. Recent advances in single-molecule junction techniques have enabled direct investigation of charge transport in a quasi-one-dimensional conduction channel composed of an individual molecule. One of the main research focuses over the past decade has been to understand the conductance switching effect of single molecules as it is essential for developing molecular-scale optoelectronics, computing, and sensing applications. In this perspective, we highlight the established physical and chemical mechanisms for single-molecule conductance switching behavior and examine the associated stimuli in single-molecule junction systems.

Introduction

Probing how electrons migrate through single molecules, which is the focus of molecular electronics (ME), offers opportunities to achieve unprecedented device functionalities that originate from the remarkable structural diversity, self-assembly capability, and the quantum nature of nanoscopic molecular structures. Meanwhile, downscaling electronic circuitry to the molecular level represents the ultimate device miniaturization and holds promise for overcoming the bottleneck with conventional solid-state devices. To enable direct quantification of the electrical properties of single molecules, researchers have developed a variety of experimental methods over the past two decades. To date, the most reliable approach features the repeated construction of a single-molecule junction (SMJ), i.e., a nanostructure in which a molecule is connected to two conductive electrodes. SMJs can be created using several techniques, including scanning tunneling microscopy break junction (STMBJ),[1–4] mechanically controlled break junction (MCBJ),[5–8] graphene-molecule-graphene junction (GMGJ),[9–11] and electromigrated break junction (EBJ).[12,13] Using these techniques, researchers have interrogated the detailed structure–property relations of a broad spectrum of molecular species by measuring their electrical conductance. Recent technical advances in combining the SMJ platform with versatile external modulations further enabled the investigation of how the physical and chemical properties of molecules respond to different perturbations, which opens the door to systematically tailor the transport properties and examine physical phenomena dominated by quantum effects. For instance, many intriguing transport behaviors have been reported in recent studies, including but not limited to transistor effect,[14,15] quantum interference,[16,17] Kondo effect,[18,19] thermoelectricity,[20] piezoelectricity,[21] biosensors,[22,23] plasmonics,[24] and spin-sensitive devices.[25,26]

One of the primary goals in ME is to create molecular switches that can cycle through the "on" (high conductance) and "off" (low conductance) states in a controlled manner because such function is pivotal for the development of molecular-scale computing, sensing, and memory devices. Therefore, it is essential to develop strategies to switch the conductance of a single molecule stably and reversibly between two or even more states.[27] Our current understanding established from SMJ studies is that in analogy to conventional electronic switches, the conductance of a single molecule can be switched via appropriate external stimuli. So far, a variety of external excitation has been applied in SMJs, such as mechanical modulation,[28–30] chemical reactions,[31–33] electrochemical and electrostatic gating,[34,35] light,[36–38] and magnetic fields.[39–41] Figure 1 illustrates several representative stimuli that have been used to generate conductance switching in SMJs. In general, these stimuli act to perturb the energy alignment of an SMJ stochastically or controllably in distinct ways, such as altering the molecular conformation,[42,43] breaking the chemical bond,[44,45] changing the molecule–electrode coupling,[46,47] or varying the spin state.[48,49] A specific focus of recent endeavors is to gain fundamental insights into the switching mechanisms and search for promising molecular candidates. Equally important is the rational design of the device architectures to enable efficient coupling of the external stimuli with the

Haixin Zhang and Mehrdad Shiri have contributed equally to this work.

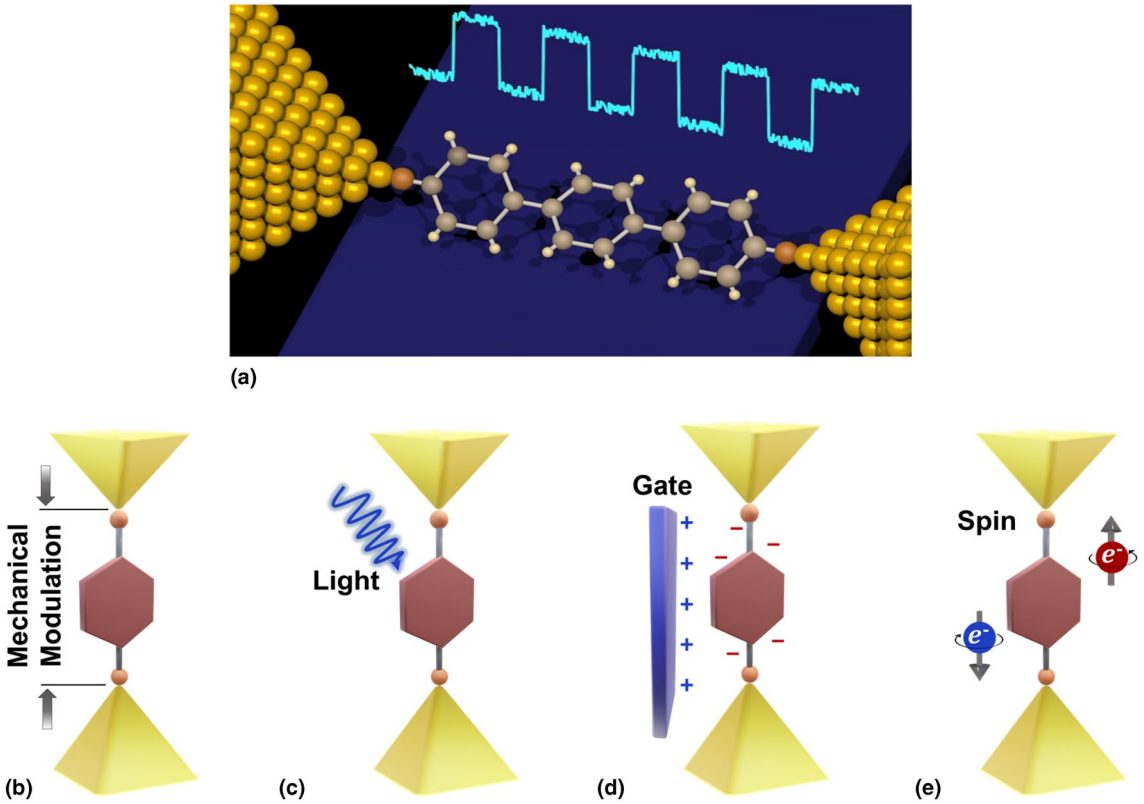

Figure 1. (a) Schematic demonstration of a single-molecule switch. The schematics highlight the typical testbed for conductance measurement and four different switching processes covered in this prospective article, namely (b) mechanically induced conductance switching, (c) bond dissociation and formation, (d) gating, and (e) spin switching.

molecular orbitals. Noticeably, the switching performance needs to be evaluated based on several critical parameters, including on/off ratio, responsivity, thermal and mechanical stability, and reproducibility. In this perspective, we highlight recent advances in probing the single-molecule conductance switching effect. We pay particular attention to the fundamental switching mechanisms that were discovered in recent SMJ studies. We also survey representative experimental techniques and the applied external stimuli. Overall, we aim to provide a molecular-level understanding and discuss the potential implications of these insights in many related areas even beyond ME, including synthetic chemistry, energy conversion, and life science. The rest of the article will be divided into multiple sections elaborating on specific physical or chemical mechanisms. We will conclude by discussing the emerging opportunities and existing challenges. In Table I, we provide a comparison among different conductance switching mechanisms, suitable experimental techniques, and addressability.

Mechanically induced conformational change

The unique advantage of the break junction approach adopted in the STMBJ and MCBJ techniques is that it allows angstrom-level control of the separation between the two electrodes in an SMJ. This has enabled the investigation of how charge transport through molecules responds to mechanical force. It has been observed that molecular conductance can be effectively tuned by mechanical modulations, namely a mechano-resistive effect.[50] Such phenomenon can arise from several sources, including the molecule–electrode interface,[51] the molecular backbone,[52] the molecular side group,[53] and intermolecular interactions.[54] Once an SMJ is formed, a typical mechanical modulation is alternating compression and elongation of the junction. Such modulation often results in a conformational change of the molecule sandwiched in the junction, leading to a conductance variation. In what follows,

Table I. Comparison of different mechanisms for single-molecule conductance switching behavior.

Mechanisms and Stimuli	Suitable Techniques		Addressability
Mechanically induced conformational change	STMBJ, MCBJ	Straightforward	It is relatively easy for the break-junction-based techniques to achieve sub-angstrom-level control of the junction separation
Bond dissociation and formation due to redox reaction	STMBJ, MCBJ, GMGJ	Sophisticated	It involves the integration of the electrochemical liquid cell into the measurement setup and requires the suppression of leakage current from the liquid
Light-driven bond dissociation and formation	STMBJ, MCBJ, GMGJ	Sophisticated	It requires integration of optical excitation to the single-molecule junction setup and aligning and focusing the external light beam to the single-molecule junction can be difficult
Environment-induced bond dissociation and formation	STMBJ, MCBJ, GMGJ	Sophisticated	It involves the integration of the liquid cell into the measurement setup and requires the suppression of leakage current from the liquid
Electrostatic gating	STMBJ, MCBJ, EBJ, GMGJ	Challenging	Fabrication of a physical gate electrode close to the single-molecule transport channel remains a technical challenge
Electrochemical gating	STMBJ, MCBJ, GMGJ	Sophisticated	It requires the integration of the electrochemical liquid cell and bipotentiostat into the measurement setup and requires the suppression of leakage current from the liquid
Spin switching	STMBJ, MCBJ, GMGJ	Sophisticated	Many spin-related phenomena are only accessible at low temperature and in high vacuum condition. It also requires either spin-injection using ferromagnetic electrode material or usage of the external magnetic field

we present recent progress in generating conductance switching behavior via mechanically manipulating the molecular conformation.

As a notable early effort, Quek et al.[55] reported that the conductance of a molecule can be reversibly switched between digital states. Utilizing the STMBJ method and statistically analyzing the most often occurring conductance, they identified two distinctive conductance states for 4,4′–bipyridine [Fig. 2(a)]. As shown in Fig. 2(b), the conductance was successively switched between high and low states, yielding an on/off ratio of ~ 10. A 2 Å displacement upon elongation can suppress the molecular conductance as low as 10^{-4} G_0. Further theoretical and experimental investigations elucidated that the two discrete conductance states are dictated by pyridine-gold contact geometry. Backed by first-principles calculations, the conductance could drastically drop as the nitrogen–gold bond becomes orthogonal to the π-system. Similar conductance switching behavior was also reported in the oligophenylenedithiol molecules by Ramachandran et al.[56] Their STMBJ measurement results showed that the conductance was switched between two distinct states as the binding configuration at the metal–molecule interface changes in response to the mechanical modulation. The high conductance state is assigned to the contact coupling between phenylene π-orbital and the gold electrode, while the low conductance state is a result of charge transport through the thiol–gold binding. Furthermore, performing a similar measurement on a family of planarized 4,4′-dipyridyls, Ismael et al.[53] showed that electromechanical switching can be effectively controlled by adding side-groups. Among the molecules studied in this work as shown in Fig. 2(c), the conductance of molecules 3 and 4 remained unchanged during mechanical modulation. This behavior was assigned to the steric hindrance caused by alkyl side-groups substituents which inhibit the switching mechanism previously reported [Fig. 2(e)]. However, molecule 2 shows a different conductance state due to different Au–N geometries [Fig. 2(d)]. The two conductance states in molecule 5 were explained by the fact that the π-conjugated side-groups interact directly with the Au contacts to establish a new transmission pathway.

Applying mechanical force to oligosilane and oligogermane wires, Su et al.[42,57] observed a pronounced conductance change owing to the stereoelectronic mechanism in which the relative orientation of orbitals affects the energy alignment. Statistical analysis on $[Si]_n$ and $[Ge]_n$ backbone with different lengths n = 1:10 resulted in the same conductance decay constant (β). This behavior firstly shows an off-resonant coherent tunneling and secondly shows the similarity of the Si–Si and Ge–Ge σ-bond in charge transport which both dominate the conductance of the C–C σ-bond. Through mechanical elongation, both molecules showed a counterintuitive conductance increase from 2.5×10^{-4} G_0 to 9×10^{-4} G_0 for Si_3 and 9.9×10^{-4} G_0 to 1.1×10^{-3} G_0 for Ge_3. 2D histograms in Fig. 3(a) and (b) clearly depict the two distinct plateaus in Si_4 conductance traces and the switching behavior of Si_6,

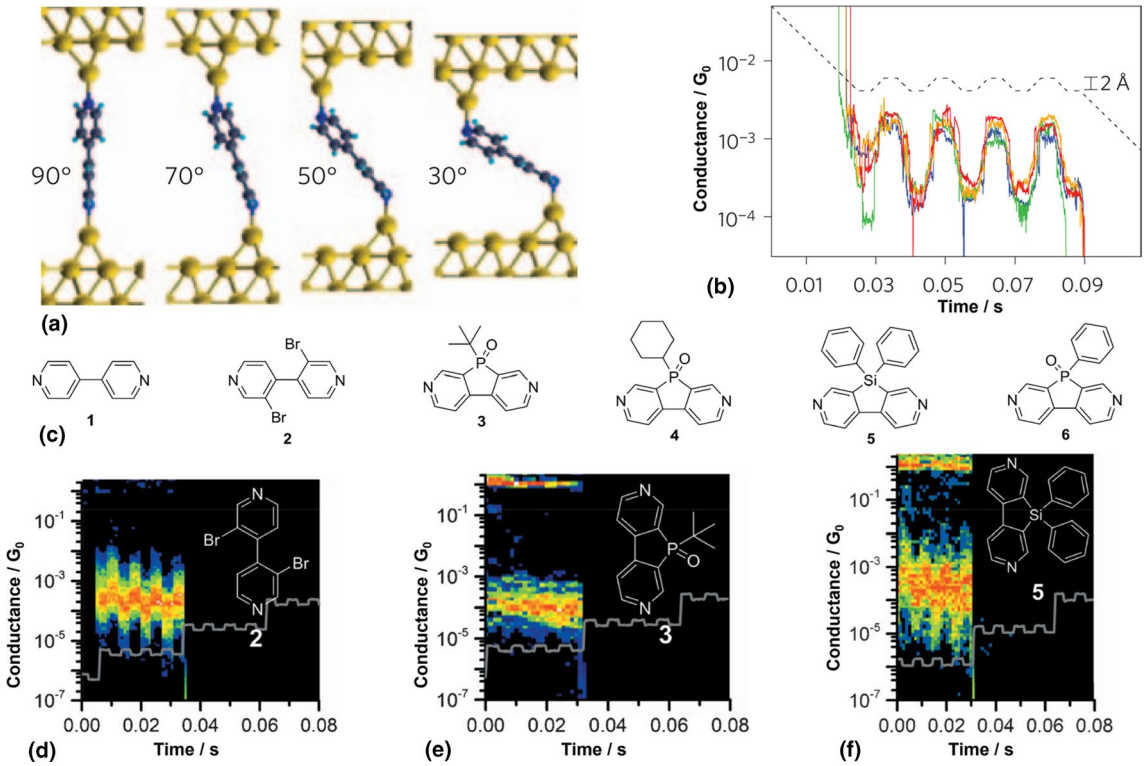

Figure 2. (a) Schematic of a single 4,4′-bipyridine molecular junction with different angles between Au (111) adatoms. (b) Conductance switching due to mechanical modulation on bipyridine (colored solid line). The traces were captured when the nonlinear ramps (dashed black line) were applied. Reproduced with permission from Ref. 55. Copyright 2009 Springer Nature. (c) 4, 4′-bipyridine molecular structure and other compounds with different side-groups. 2D histogram of conductance vs. time for the molecule (d) 2 (f) 3 (g) 5 in addition to the gray line showing the tip displacement. Reproduced with permission from Ref. 53. Copyright 2017 John Wiley and Sons.

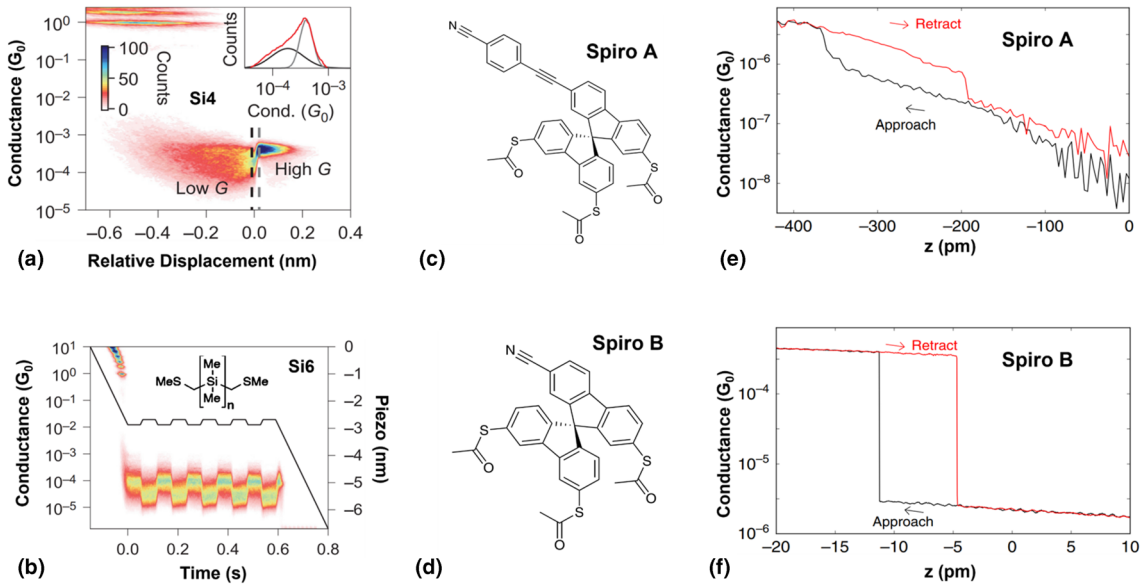

Figure 3. (a) 2D conductance histogram of $[Si]_4$ measured from traces exhibiting conductance switching. The inset in a) represents the conductance 1D histogram in off state (black curve), on state (gray curve), and superimposition of all traces. (Red curve). (b) Conductance variation of $[Si]_6$ during successive compression and elongation. Reproduced with permission from Ref. 42. Copyright 2015 Springer Nature. The molecular structure of (c) Spiro A and (d) Spiro B. The current through (e) Spiro A and (f) Spiro B as a function of piezo displacement for different moving directions. Reproduced with permission from Ref. 58. Copyright 2016 Springer Nature.

respectively, during compressions and elongations. Supported by calculations, it was shown that the stereoelectronic properties of Me–S σ-bond were coupled by the silane backbone at the electrode interface, causing three dihedral conformations with different conductances.

Deeper conductance suppression has been achieved by a molecule immobilized on tripod nitrile family anchors holding a freely suspended arm consisting of Spirobifluorene derivatives (Spiro).[58] As shown in Fig. 3(c) and (d), two molecules with the same backbone have been compared and a fully controllable switch has been realized using STMBJ at low temperatures. Spiro A has an additional aromatic ring in the former position of the nitrile group Spiro B. As shown in Fig. 3(e) and (f), upon mechanical elastic deformation, the I–z curve exhibits a hysteresis effect. During the mechanical modulation, the high conductance for both molecules occurs upon tip approaching (i.e., junction compression) and switches back to the low conductance during tip retraction (i.e., junction elongation). For Spiro B, as the more conductive molecule, a significant conductance change by more than two orders of magnitude was observed. Based on DFT calculations, two equilibrium states with different conductance (i.e., the observed current hysteresis) were attributed to distinct junction conformations induced by the free-moving tripod-like S atoms on the gold substrate during the mechanical modulation of the tip position. It is expected that the energy surface of the tip exhibits a double-well potential (one for the ON state and the other for the OFF state), of rather similar energy but separated by an energy barrier. The mechanical modulation of the junction separation assists to overcome the energy barrier between the two states, thus leading to the conductance switching behavior. The switching behavior was also reported in the same work when a voltage above a certain threshold was applied. The lateral positioning of the tip, hovering over the nitrile arm, determines the necessary electric field intensity to toggle the switch. The induced electric field creates a torque that moves the suspended arm. Responsivity and bistability of on and off states can make avenues for flip flops or memristive devices with trigger pulses as short as 130 μs.

In another work, a room-temperature conductance switching was achieved by applying a shear force to the π-stacking spring-like molecule of paracyclophane (PC) [Fig. 4(a)].[59] One order of magnitude conductance increase on both compression and stretching was conceptualized through shifting the conductance out of transmission anti-resonance of 3.7×10^{-6} G_0 caused by destructive quantum interference (DQI). Figure 4(b) illustrates the three conductance states resulting from elongation, no force, and compression. Verified by the DFT ab initio calculations, the anti-resonant valley in the transmission is shifted by moving the molecular orbitals out of symmetry as the molecule is stretched or compressed. Under no force, the Fermi energy lies close to the anti-resonance stemming from the DQI of the HUMO and LUMO. Once displacement is applied, it breaks the orbital symmetry and brings about the pair degeneracy of HOMO-1, HOMO, LUMO-1, and LUMO, which eventually disables the DQI effect.

Moreover, Wu et al.[54] exploited the interchangeable *anti-syn* conformation for switching of flexible diketone [Fig. 4(c)]. In this work, the torsional barrier was overcome and relaxed between two equilibrium states by mechanical folding and unfolding. The difference in the conductivity between two dihedral angles was realized by intramolecular π–π interactions. In other words, tunneling through space "bypasses" the molecular backbone in the folded conformation, resulting in a 21-fold increase in the conductivity [Fig. 4(d)]. DFT calculations confirmed that this effect arises solely from π–π interactions deliberately brought close together in the *syn* (folded) form. Additionally, Li et al.[60] have shown that through-space interactions can compensate for the weak through-bond charge transport in the highly twisted backbone of ortho-polyphenylene. The conductance of the twisted molecule can be mechanically tuned by two orders of magnitude as multiple transport pathways become accessible through space and bond conjugation.

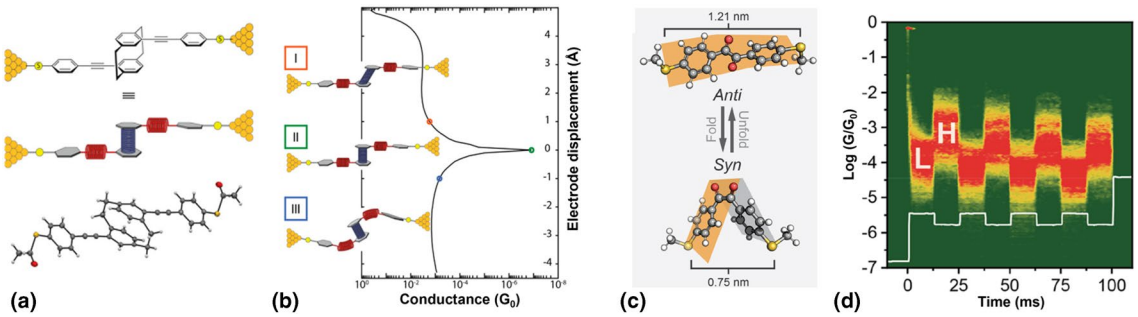

Figure 4. (a) Schematic for mechanical break junction measurement performed on the OPE-linked PC molecule along with the spring system analogy, and (bottom) Molecular structure obtained by X-ray analysis. (b) Conductance variation of the molecule subject to I) elongation II) no force III) compression based on DFT calculations. Reproduced with permission from Ref. 59. Copyright 2018 Chemical Society. (c) Schematic for molecular structure when undergoes a transition from anti to syn and vice versa along with S–S distance. (d) Density map of conductance during 5 successive compressions and elongations. Reproduced with permission from Ref. 54. Copyright 2020 American Chemical Society.

Taking advantage of the low rotational energy barrier of cyclopentadienyl (Cp) rings in ferrocene derivatives, Camarasa-Gomez et al.[61] have shown that the conductance can be mechanically modulated by 2 orders of magnitude. In this work, a single molecule consisting of a ferrocene molecule connected to two thioanisole at both ends forms the junction in the STMBJ setup. Theoretical investigation elucidated that the rotation-dependent DQI arising from a change in the hybridization between delocalized Fe d-orbital and ligands π-system contributed to the conductance switching. In a similar work, Pei et al.[62] studied a molecule featuring ferrocene as a hinge between two pyridyl-terminated alkynyl arms, attached to the Cp rings in the 1,1' positions. Under mechanical modulation, this molecule yielded conductance switching between two discrete states with an on/off ratio as high as 200. Mechanical elongation of the junction induced rotation of the anchoring group and, subsequently, dihedral angle between two alkyne side arms changes, leading to a higher conductance due to a more delocalized orbital around the tip (higher coupling strength). On the other hand, the junction compression results in symmetry breaking (or less hybridization) and decreases the conductance. Clearly, these recent results have demonstrated the potential of integrating molecular components into nanomechanical systems.

Bond dissociation and formation

In an SMJ, chemical bonds along the molecular backbone form the foundational pathway for electrons. Therefore, perturbing the chemical bonds has been considered a viable approach to turn electron transmission on or off through molecules, also known as the bond switching mechanism. To date, harnessing the intrinsic properties of specific molecules, researchers have explored a variety of stimulation strategies, such as redox reaction, optical excitation, and environmental control. These stimuli have been shown to induce bond rupture, formation, and/or rotation within the molecular backbone. These bond alterations are often reversible, thus suitable for creating conductance switching behavior. In this section, we discuss some of the representative bond cleavage and formation mechanisms categorized based on the applied stimuli.

Redox reaction

An effective way to significantly alter the molecular bonds is to induce a redox reaction in the molecular core that dominates the charge transport.[47,63–65] Similar to conventional cyclic voltammetry measurements, the redox reaction for a single molecule can be activated in an SMJ setup.[66–68] This is typically achieved in a four-electrode electrochemical cell, with the source and drain electrodes of the SMJ being the working electrodes and the counter and reference electrodes alongside. A redox reaction can be triggered via sweeping the electrochemical potential for the molecular junction immersed in an electrolyte solution. Molecular electrical measurements have been used to monitor the detailed reaction processes particularly in redox-active molecules including viologens,[69] ferrocenes,[70] anthraquinones,[71] polyaromatic hydrocarbons,[72] polyoxometalate,[73] as well as organic radicals.[74] It has been shown that redox reactions can lead to pronounced conductance switching when a redox-active molecule is used as the conduction channel.

Yin et al. recently demonstrated that the Hückel antiaromaticity effect can be leveraged to create single-molecule switches.[75] Using the STMBJ setup in an electrochemical cell, they observed conductance switching for 8,8′-biindeno[2,1-b] thiophenylidene (BTP) between two states upon the occurrence of a redox reaction. The neutral state aromatic structure yielded a low conductance, and, upon electrochemical oxidation, it reversibly switches to an antiaromatic high-conducting structure [Fig. 5(a)]. After the oxidation, the aromatic neutral TBTP molecule [Fig. 5(b)] loses two electrons, becoming a dication of the antiaromaticity. As shown in Fig. 5(c), due to the redox activity of BTP, alternating the gate voltage between a negative value (<-1.5 V) and a positive value (>1 V) led to a conductance switching between the on and off states with an on/off ratio of ~70. This significant conductance rise is attributed to a partial resonance transmission that was created close to the electrode Fermi energy. In another work by Kay et al., a multistep oxidation process was also observed using the electrochemically gated STMBJ method [Fig. 5(d)].[67] In their work, the redox-active molecular core, pyrrolo-tetrathiafulvalene incorporated with a $(CH_2)_6SAc$ group at each end (6pTTF6), was studied in a room-temperature ionic liquid (RTIL), 1-butyl-3-methylimidazolium trifluoromethanesulfonate (BMIOTf). A strong effect of the ionic liquid was shown in the measurement results [Fig. 5(e)]. Two conductance peaks corresponding to two oxidation transitions (6pTTF6 to $6pTTF6^+$ and $6pTTF6^+$ to $6pTTF6^{2+}$) were clearly demonstrated in the electrochemical potential window, while there was barely one oxidation reaction occurring in an aqueous buffer electrolyte. Although the on/off ratio of this molecular system is relatively low (~4), the sequential redox reaction provides a possible route to design more complex multistep switching functionalities at the molecular scale.

Optical stimuli

Thanks to the photoresponsive nature of a particular group of molecules (e.g., photochromic molecules and their derivatives), driving conductance switching through optical means represents another primary focus of molecular switch studies. Several photochromic molecules which are effortless to synthesize include azobenzenes,[76] dihydroazulenes,[77] and spiropyrans.[78] Light has several unique advantages over other stimuli, such as remote access, ultra-fast responsivity, energy tunability, and noninvasiveness.[38] Upon light illumination, the photoresponsive moiety of the photochromic molecules often undergoes a bond cleavage (opening) or bond formation (closing) process, leading to a drastic conductance decrease or increase, respectively.[44,79–81] A problem in early works was that only unidirectional optoelectronic switching (e.g., from

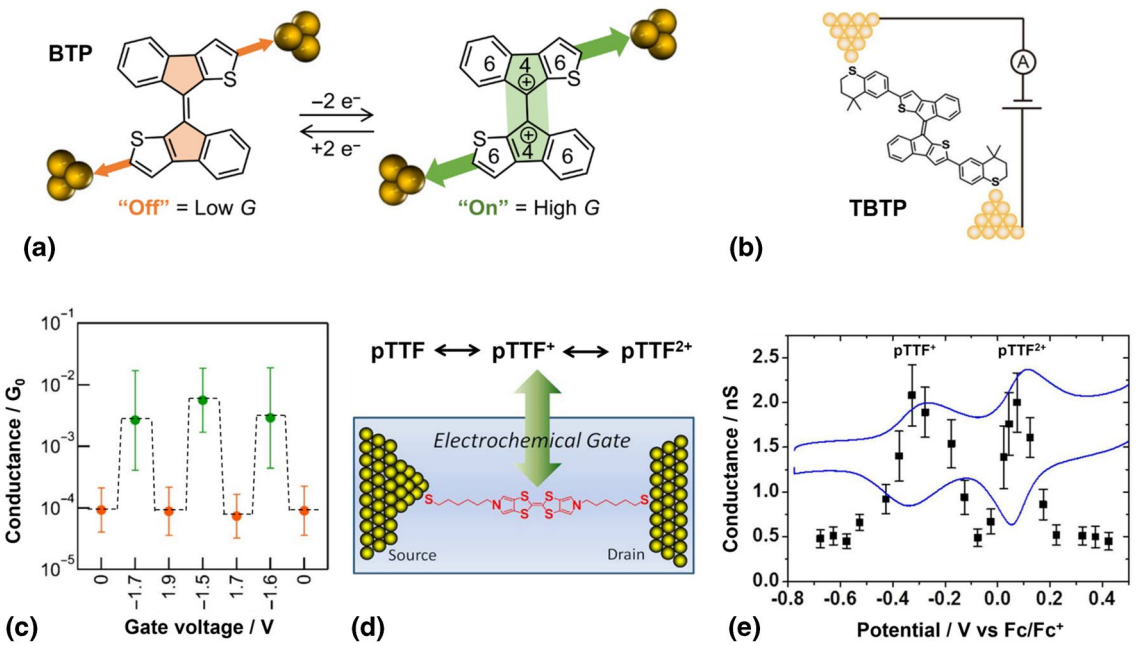

Figure 5. (a) Redox reaction in the redox-active BTP group. (b) Schematic of STMBJ measurement setup. (c) Conductance switching between two states with reversely changing gate voltage. Reproduced with permission from Ref. 75. Copyright 2017 American Association for the Advancement of Science. (d) Schematic of STMBJ setup with electrochemical gate. (e) Conductance switching of different oxidation states of 6pTTF6 molecule. The blue curve is the cyclic voltammetry result. Adapted with permission from Ref. 67. Copyright 2012 American Chemical Society.

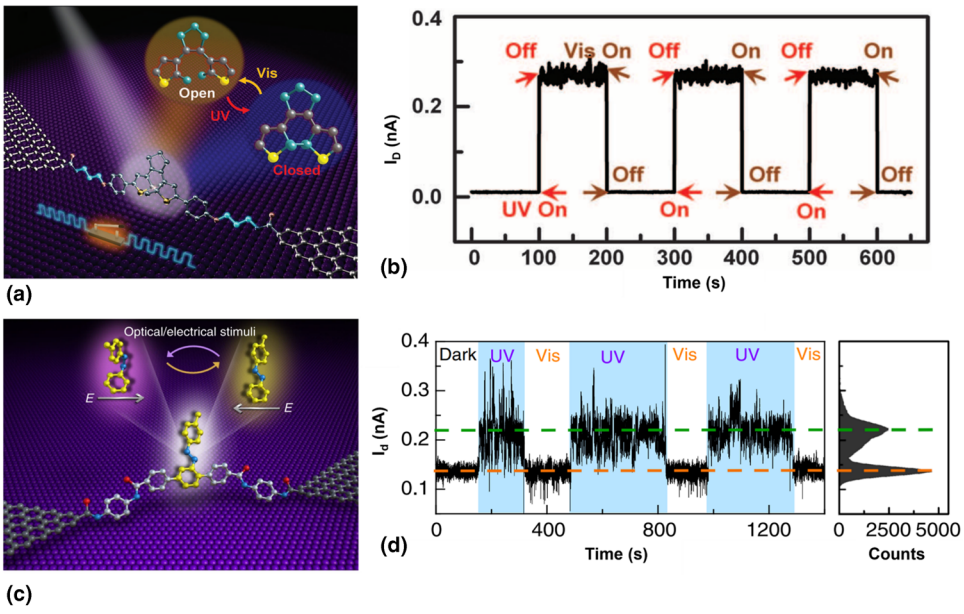

Figure 6. (a) Single-molecule junction with diarylethene molecule. (b) Conductance switching with on/off states. Reproduced with permission from Ref. 45. Copyright 2016 American Association for the Advancement of Science. (c) Molecular junction setup and isomerization of the molecule due to optical/electrical stimuli. (d) Left panel: conductance switching corresponding to cis (green) and trans (orange) states with sequential UV and visible light stimuli. Right panel: 1D histogram of the left panel. Reproduced with permission from Ref. 83. Copyright 2019 Springer Nature.

closed and on state to open and off state) was observed when using metals as the electrode in SMJs. This problem is attributed to the quenching of the molecular excited state due to strong molecule–electrode coupling. Such an issue was recently resolved when a weakened molecule–electrode coupling was established using the graphene-based electrode. In what follows, we present recent experimental studies that demonstrated promisingly stable and reversible switching behavior using the GMGJ setup.

In a notable experimental work by Jia et al.,[45] an SMJ containing diarylethene as the molecular core was elegantly studied using the GMGJ method. To facilitate a weak molecule–electrode coupling, three methylene (CH_2) groups, functioning as the spacing group between the photoresponsive molecular core and the graphene electrode, were incorporated into each side of the molecule [Fig. 6(a)]. Upon UV light excitation, the open form, where the delocalization of π electrons is interrupted by the disconnected bond, transforms to the closed form, where the completed electron delocalization covers the whole molecule [Fig. 6(b)]. This phenomenon leads to the transition from low conductance (off state) to high conductance (on state). On the other hand, when exposed to visible light, the close form switches back to the open form, leading to the transition from off to on state. The conductance switching process is highly reversible with a high on/off ratio of ~ 107. Noticeably, this single-molecule switching device exhibits an impressively long lifetime up to one year with good reproducibility, implying a nearly practical molecular device.

Using the same approach, azobenzene derivatives, as another group of photochromic molecules, were also studied recently for their photoswitching effect.[82] Meng et al.[83] investigated the 2′-*p*-tolyldiazenyl-1,1′:4,4′-terphenyl-4,4″-dicarboxylic acid (TTDA) bridging two graphene electrodes Fig. 6(c). Due to the photochromic side group of TTDA, the molecule can be isomerized between two states, *cis* and *trans*, with UV/visible light illumination. Through alternating UV and visible light excitation, they observed a reversible conductance switching between the on (*cis*) and off (*trans*) states with an on/off ratio of ~ 2.1 [Fig. 6(d)]. According to the DFT calculation, when the molecule isomerizes from *trans* to *cis*, the perturbated highest occupied molecular orbital (p-HOMO), the orbital dominating the charge transport, shifts closer to the graphene Fermi energy, increasing the conductance.

Environment-induced switching

It has also been demonstrated that varying the surrounding environment of the molecule, such as the acidity of the solution, can tailor its charge transport properties and generate conductance switching behavior.[84–87] Protonation and deprotonation, a process in which a coordinate covalent bond is formed (broken) by adding (removing) a proton, usually occur when an acid/base is introduced into the liquid.[88] These structural and chemical bond changes contribute to the distinct conjugation forms and could lead to the quantum interference effect of molecule orbitals. Thus, by using the SMJ technique, a series

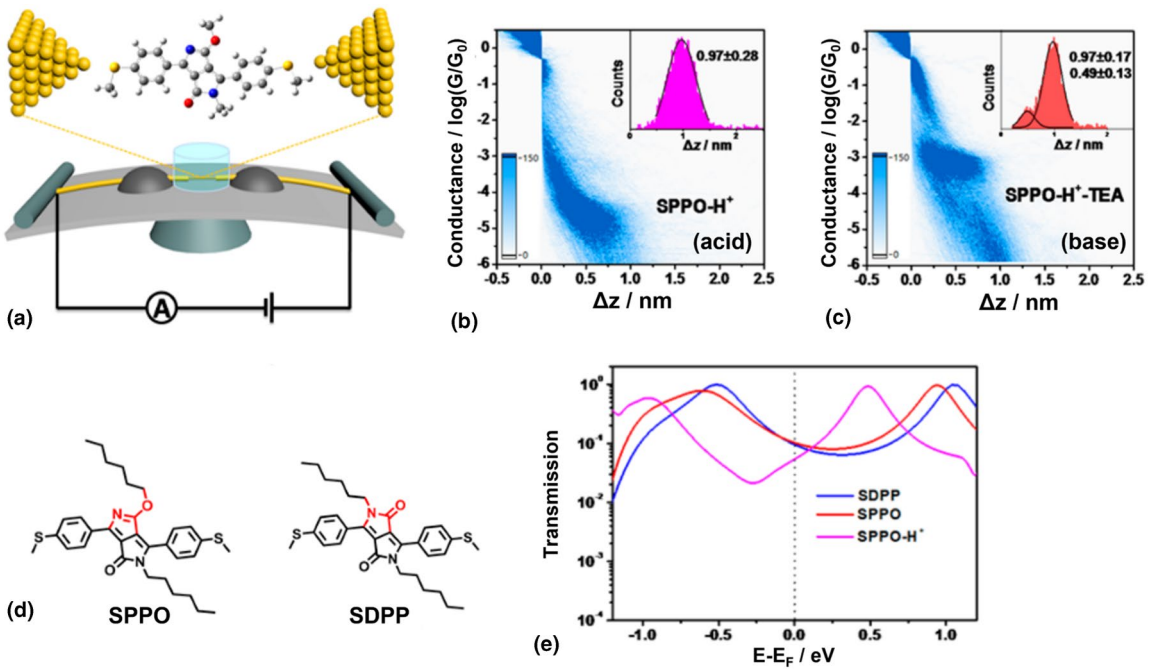

Figure 7. (a) Schematic of MCBJ measurement setup. (b) 2-D histograms of SPPO-H^+ within the acid environment. (c) 2-D histograms of SPPO-H^+-TEA molecule within the base environment. Insets of (b) and (c) are 1-D histograms of the relative distance (Δz). (d) Molecular structures of SPPO and SDPP. (e) The transmission function of molecules around Fermi energy based on DFT calculation. Adapted with permission from Ref. 92. Copyright 2018 American Chemical Society.

of pH-sensitive molecules have been investigated recently, including dye molecules,[89] pyridyl molecules,[90] and azulene derivatives.[91] For example, using the MCBJ method, Zhang et al.[92] studied diketopyrrolopyrrole (DPP) containing isomers named SDPP and SPPO [Fig. 7]. The conductance measurement results yielded undistinguishable conductance values for SDPP and SPPO. However, after introducing camphor sulfonic acid (CSA) into the solution, the conductance of SPPO decreased by one order of magnitude (namely SPPO-H^+) [Fig. 7(b)], while the conductance of SDPP remained unchanged. By further adding triethylamine (TEA) to the SPPO-H^+ solution (namely SPPO-H^+-TEA) [Fig. 7(c)], the conductance of the molecule switched back to that of the original SPPO. Such conductance response was attributed to a reversible protonation and deprotonation process of the SPPO molecule. The one order of magnitude conductance reduction was due to the DQI induced by the protonation [Fig. 7(e)]. This work suggests a switching mechanism that originates from the environment.

Gating effect

One of the crucial objectives of ME is to control the current using the third terminal without disturbing the molecular conformation or causing any chemical processes. This enables researchers to mimic the silicon-based transistor functionality at the atomic and molecular scale, where the quantum transport dominates.[35,93,94] Like what occurs in a solid-state field effect transistor, the gate voltage applied to an SMJ shifts the frontier molecular orbital with respect to the Fermi level of the electrode, thus modifying the transmission characteristics of the junction. Following this idea, Song et al. demonstrated direct tuning of the molecular orbital in 1,8-octanedithiol (ODT) and the 1,4-benzenedithiol (BDT) molecules[95] using the EBJ technique. The gate electrode buried 3 nm beneath the Al_2O_3 insulating layer effectively lowered the transition voltage, leading to the gating efficiency as high as $\alpha = +0.25$ for HOMO-mediated transport. Using a similar approach but incorporating temperature control, Kim et al.[96] further showed electrostatic gating of the electrical conductance and thermoelectric properties of single molecules at the same time. In their study, the electrostatic modulation shifted the Fermi energy toward the transmitting orbital of biphenyl-4,4′-dithiol and fullerene molecules, where both conductance and the Seebeck coefficient are enhanced.

As a promising alternative, electrochemical gating has received extensive attention in recent years. This is primarily because when an SMJ is held in an electrochemical cell, an extremely thin electrical double layer (comprising a small number of ions making the layer a few Å thick) is formed upon applying the gate voltage, ensuring enhanced interaction between the molecule and the applied electric field. Such an effect has been used to effectively tune the energy levels of the bridging molecule.[64,97–99] In an STMBJ study

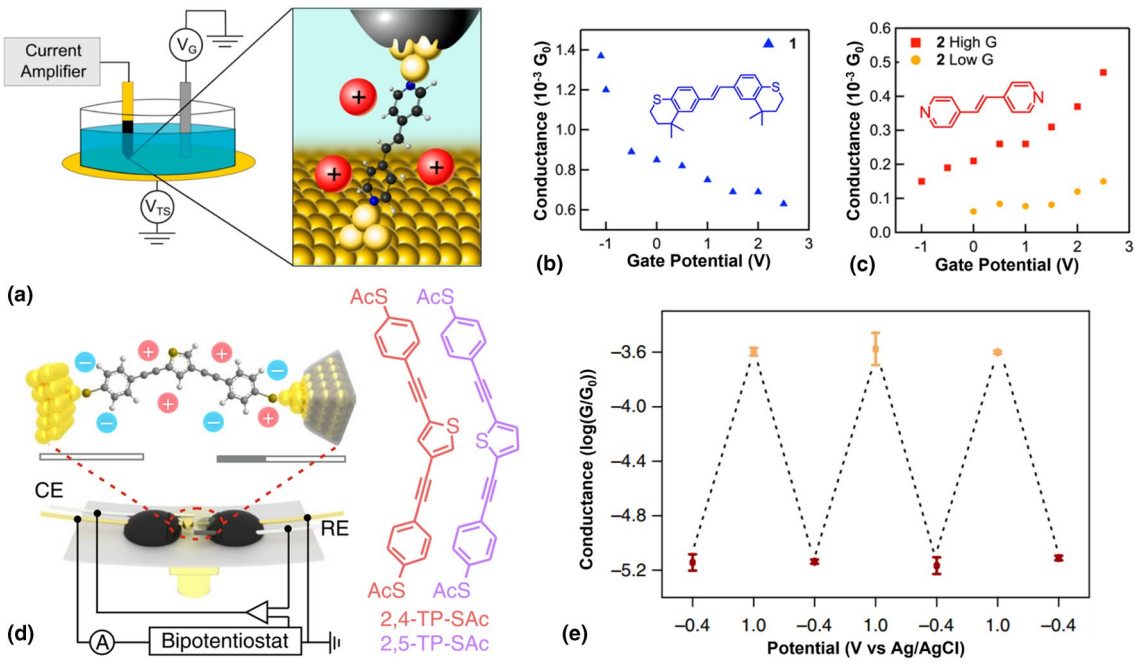

Figure 8. (a) Schematic of STMBJ measurement setup conducted in the ionic liquid cell. The conductance change as a function of applied gate voltage for (b) 1,2-bis (4,4′ dimethylthiochroman-6-yl) ethylene and (c) 1,2-bis (4-pyridyl) ethylene. Each point on (b) and (c) plots represents the peak in the 1D histogram as the most frequently appeared conductance. Reproduced with permission from Ref. 100. Copyright 2014 American Chemical Society. (d) Schematic for electrochemical gating on MCBJ experimental platform and two thiophene derivatives. (e) Reversible conductance switching of 2,4-TP-SAc under two bias voltages of – 0.4 V and 1 V with respect to Ag/AgCl electrode. Reproduced with permission from Ref. 101. Copyright 2019 Springer Nature.

by Capozzi et al.,[100] an energy shift as high as 0.8 eV was reported with this method. In this study, a positive Pt gate electrode immersed in tetrabutylammonium perchlorate electrolyte caused an accumulation of the negative ions around the molecule [Fig. 8(a)]. A constant voltage (the source-drain voltage) was then applied between the wax-coated Au tip and Au substrate. Two molecules studied in this system, namely 1) 1,2-bis (4,4′ dimethylthiochroman-6-yl) ethylene and 2) 1,2-bis (4- pyridyl) ethylene. Figure 8(b) and (c) demonstrates the conductance change as a function of gate voltage for molecules 1 and 2, respectively. Further increasing the gating efficiency to 100% in the STMBJ setup and KClO liquid cell, Baghernezhad et al.[66] showed a reversible conductance switching by one order of magnitude over a 1 V gating window. However, the marginal conductance change has occurred in the redox-inactive region, and a sudden change took place by increasing the voltage to the redox-active region of the molecule.

As mentioned earlier, the prominence of quantum transport of charges in the molecular channel gives rise to promising flexibility absent in conventional transistors. Arising from the wave nature of the electron, the intriguing phenomena of DQI can lead to high on/off ratios and high thermoelectric efficiency. In an MCBJ setup shown in Fig. 8(d), Bai et al.[101] experimentally showed that the molecule's energy levels could be adjusted *in situ* by electrochemical gating in the non-faradaic region. To achieve high switching ratios, they selected thiophene core molecules with thioacetyl (–SAc) anchoring group (2,4-TP-SAc), which showed DQI in the vicinity of the Fermi energy. Applying voltage from -0.4 V to 1.3 V with respect to Ag/AgCl quasi-reference electrode suspended in the ionic solution, the transmission anti-resonance was shifted away from the Fermi energy resulting in two orders of magnitude conductance surge from $10^{-5.1\pm0.02}$ G_0 to $10^{-3.2\pm0.07}$ G_0, as illustrated in Fig. 8(e). Substantiated by DFT calculation, without any redox reaction taking place, the 2,4-TP-SAc molecule with DQI has one order of magnitude higher switching ratio than that of 2,5-TP-SAc without DQI.

Recently, three different heterocyclic rings, incorporated in dihydrobenzo[b]-thiophene (BT) molecule, have been studied to achieve high gating efficiency.[102] The electrochemical potential in a 1.2 V window was swept to build the transmission curve in the STMBJ. The molecular junction was immersed in the electrolyte solution of 1-butyl-3-methylimidazolium hexafluorophosphate (BMIPF 6). From Statistical analysis, the conductance increased gradually from initial values of 6.3×10^{-5} G_0, 8.9×10^{-5} G_0, and 1.2×10^{-4} G_0 at -0.9 V gate voltage for furan (BT-O), thiophene (BT-S), and selenophene (BT-Se), respectively. The relatively high conductance gating ratio reported in this work is BT-Se (1000%)>BT-S (708%)>BT-O (635%)>BT-C (282%), evidencing the fact that the electronic structure of heterocyclic rings can remarkably enhance the gating performance.

Apart from the mentioned three-terminal molecular switching devices, it has been shown that single-molecule conductance can exhibit a considerable non-linearity in two-terminal devices as a demanding feature in modern electronics. Bias-driven conductance change was recently explored in fluorene oligomers incorporating a central benzothiadiazole. By adding up to three oligofluorene units on both sides of benzothiadiazole, Greenwald et al.[103] decreased the energy level spacing between highly coupled successive molecular orbital with opposite phase causing DQI to occur close to Fermi level of the electrode. This, consequently, resulted in considerable suppression of conductance by 4 orders of magnitude. In the I-V measurements conducted using STMBJ at room temperature, the conductance obtained at high bias (2 V) is ~10,000 times more than that at low bias (0.5 V), which accents the high non-linearity of the device.

Spin switching

The spin state of electron has also been manipulated to achieve reversible switching between stable states with different conductance. The realization of such spin switching at the single molecule level promises excellent novelty in the field of spintronics and quantum information.[104] For example, Wagner et al.[105] showed that spin-dependent charge transport could be achieved by tailoring a molecular complex in which the magnetic coupling of the spin pair ion of Co^{2+} is perpendicular to the charge transmission channel. As depicted in Fig. 9(a), using the MCBJ platform, they measured the transmission through co-planar bipyrimidine ligand modified with two Co^{2+} on preferential axis to electrically switch the molecule between low conductive pseudo-singlet and high-conductive pseudo-triplet. Based on the I-V curves, the bridging molecules were termed type 1 and type 2. For type 1 molecular junctions, the peak of the dI/dV curve increased up to the saturation point by decreasing the temperature, because of zero-bias anomaly (ZBA), as expected for the Kondo effect in low temperature. In addition, with external magnetic field applied, the zero-bias peak splitting was observed for the type 1 bridge, which implies a pseudo-triplet state. The I–V and dI/dV–V measurement results on types 1 and 2 are depicted in Fig. 9(b) and (c), respectively. An abrupt transition at $\mp$0.2 V was observed. This region manifests a non-magnetic pseudo-singlet state where no magnetic response is expected. For down-sweep and up-sweep bias voltages, the hysteric I–V curve was reported for coupled spin pair, which indicated switching from non-magnetic singlet to magnetic triplet at certain applied voltages.

Moreover, electric field-induced spin switching was also realized on the single $[Fe^{II}(tpy)_2]$ complex, functionalized orthogonally on spin-crossover compound [Fig. 9(d)].[48] Through MCBJ measurements, reversible switching from low to high conductance state was observed due to the spatial arrangement of the intrinsic dipole moment of terpyridine ligands. In this study, the applied electric field leads to distortion of the Fe^{II} coordination sphere, which changes the spin state. The discontinuities in the I–V curves at around 0.7 V and –0.5 V imply the hysteretic behavior of the device. Analyzing

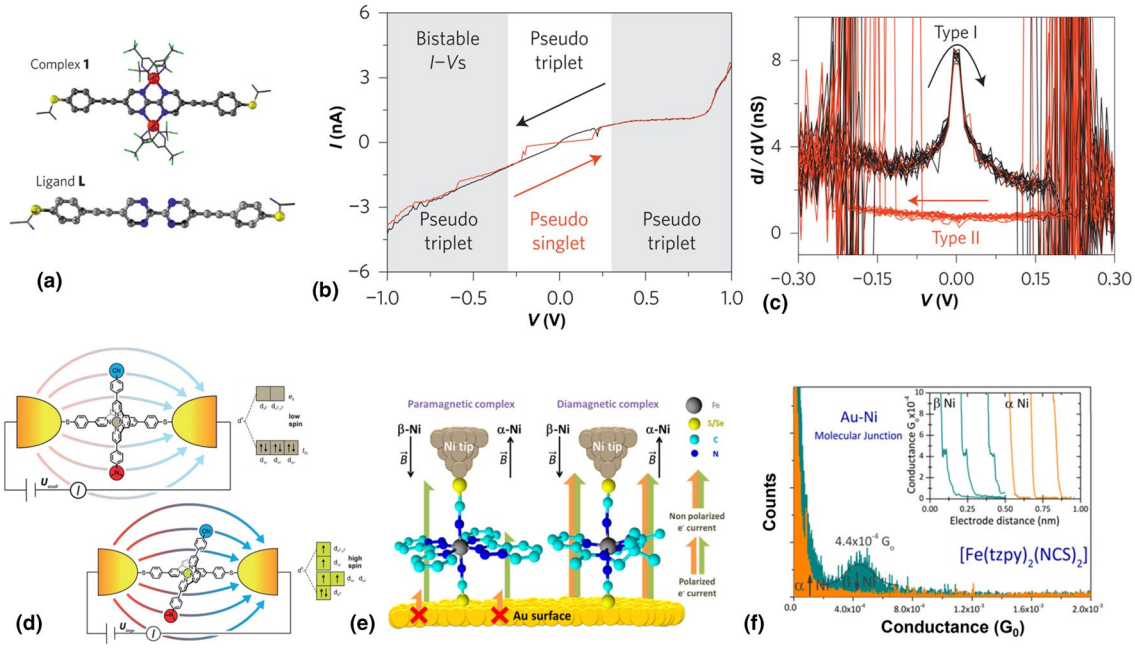

Figure 9. (a) Molecular structure of the bipyrimidine and complex 1 incorporating Co^{2+} which is designated by red spheres. (b) hysteric behavior of the coupled spin pair shown in bistable I–V curve. (c) Current derivative for different applied bias voltages. The arrows represent the sweeping direction of applied bias. Reproduced with permission from Ref. 105. Copyright 2013 Springer Nature. (d) Schematic of spin-crossover molecule exposed to the electric field. Top: low spin Fe^{II} in a weak electric field. Bottom: distorted coordination sphere owing to the strong electric field and dipole realignment. Reproduced with permission from Ref. 48. Copyright 2015 John Wiley and Sons. (e) Schematic illustration of single-molecule junction bridging Ni contacts with α and β magnetic polarizations. Left: $[Fe(tzpy)_2(NCS)_2]$ complex showing spin-dependent transmission. Right: Diamagnetic $[FeL^A(NCS)_2]$ molecule exhibiting no dependence upon magnetic polarization of the contacts. (f) 1D conductance histogram for $[Fe(tzpy)_2(NCS)_2]$ complex in α and β magnetic polarizations. Inset: typical conductance traces for both magnetic polarizations. Reproduced with permission from Ref. 49. Copyright 2015 American Chemical Society.

all junctions trapped between the electrodes, various current profiles were observed without hysteresis due to the molecule's random orientation with respect to the electric field.

Nevertheless, all measurements above have been carried out at low temperatures using non-magnetic contacts. Adopting Ni as ferromagnetic material in an STMBJ setup, Aragones et al.[49] reported two orders of magnitude increase in the conductance of spin-crossover complex $[Fe(tzpy)_2(NCS)_2]$. As shown in Fig. 9(e), the conductance has been actively controlled by changing the magnetic polarization of the Ni tip from α orientation to β, the behavior that was absent in the diamagnetic complex $[FeL^A(NCS)_2]$. The 1D histogram in Fig. 9(f) shows the conductance quenching of the $[Fe(tzpy)_2(NCS)_2]$ molecule from 4.4×10^{-4} G_0 to well below the noise floor upon changing the magnetic polarization from α to β. The spin-dependent charge transport has been ascribed to the spin selectivity of the S–Au bond. Such effect was also attributed to the high-spin S = 2 Fe^{II} of the complex that partially blocks the spin-selected majority carriers (β-spin), and the enhancement of minority carrier current by the correctly chosen magnetic polarization of the Ni tip. It is evident that these recent signs of progress in harnessing electron spins in single molecules have laid out a solid foundation for future molecular spintronics.

Conclusion and outlook

In this article, we have highlighted several promising physical mechanisms and the associated external stimuli that can be leveraged to create conductance switching behavior in single molecules. We have discussed how novel SMJ techniques are employed as powerful tools for single-molecule manipulation under controlled environmental conditions. Together, research progress made over the past decade has underpinned the suitability of using single molecules as reliable and controllable electronic devices. As a notable example, a highly stable single-molecule switch fabricated in the graphene-molecule-graphene junction can now retain the switching stability and reproducibility over a year, implying a nearly practical molecular device for real-world application. In addition, at the fundamental level, insights from conductance switching studies have also profoundly advanced our knowledge of quantum transport in molecular systems. There is no doubt that a deep understanding of the interplay between physics and chemistry at the molecular scale will pave the path toward the design and engineering of novel device functionalities and complexities that were unimaginable before, especially when the quantum effects of molecules can be comprehensively exploited.

Despite the recent progress, challenges remain to be addressed in several aspects. One of the outstanding issues is the mechanical and thermal stability of SMJ switching devices. This issue is often attributed to the variation of the molecule–electrode contact geometries driven by mechanical or thermal fluctuation over time. Hence, to improve the junction stability, a better design of the molecule–electrode contact chemistry and binding strategies is needed. A more stable SMJ would also enable the characterization and improvement of the switching response rate, which is difficult to access using the break junction-based methods. Another limiting factor is the on/off ratio. Although high on/off ratios (> 100) have been observed in some molecules, most molecular species suffer from moderate on/off ratios (< 20). It is important to rethink how to greatly enhance the conductance of the "on" state while suppressing the "off" state. A possible solution is to harness the molecular quantum interference effect.[16,94,99] To move forward with this approach, an integrated effort from synthetic chemists, theoreticians, and experimental physicists is necessary. Practical application of molecular-scale devices also requires good device scalability. A viable route to scale up molecular devices is to take advantage of the self-assembly abilities of molecules. To this end, the recent development of scalable molecular architectures, such as supramolecules and artificial molecular machines, deserves more in-depth investigation. Furthermore, with several powerful single-molecule techniques available, now is the time to increase the complexity of SMJ systems from all aspects, including the molecule, the electrode, and the overall device architecture. For instance, coupling molecules with emerging two-dimensional quantum materials or energy harvesting materials could be a promising next step.

Finally, single-molecule conductance switching studies have a broad impact in many areas beyond ME. The ability to monitor the electrical signals of single molecules is essential for investigating fundamental chemical (e.g., chemical reactions and catalysis)[106–109] and biological (e.g., protein binding and DNA sequencing)[110–112] processes. It is also expected that the developed experimental platforms will provide a suitable route to gain molecular-level insights into crucial energy-related processes in emerging materials, such as perovskites, organic light-emitting diodes, conductive conjugated polymers, and plasmonic nanostructures.[113] We anticipate that the incorporation of SMJ techniques into these areas may uncover previously hidden material properties and catalyze new research directions in the future.

Acknowledgments

We gratefully thank the financial support from the U.S. Department of Energy, Office of Science, Basic Energy Sciences under Award No. DE-SC0021942 and National Science Foundation under Award No. OIA-1757220.

Data availability

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of interest

All authors declare that they have neither financial nor personal interests that could affect the manuscript and results.

References

1. S. Guo, G. Zhou, N. Tao, Single molecule conductance, thermopower, and transition voltage. Nano Lett. **13**, 4326–4332 (2013)
2. N.J. Tao, Electron transport in molecular junctions. Nat. Nanotechnol. **1**, 173–181 (2006)
3. C. Li, I. Pobelov, T. Wandlowski, A. Bagrets, A. Arnold, F. Evers, Charge transport in single Au | alkanedithiol | Au junctions: coordination geometries and conformational degrees of freedom. J. Am. Chem. Soc. **130**, 318–326 (2008)
4. V. Kaliginedi, P. Moreno-García, H. Valkenier, W. Hong, V.M. García-Suárez, P. Buiter, J.L.H. Otten, J.C. Hummelen, C.J. Lambert, T. Wandlowski, Correlations between molecular structure and single-junction conductance: a case study with oligo(phenylene-ethynylene)-type wires. J. Am. Chem. Soc. **134**, 5262–5275 (2012)
5. D. Natelson, Mechanical break junctions: enormous information in a nanoscale package. ACS Nano **6**, 2871–2876 (2012)
6. D. Xiang, H. Jeong, T. Lee, D. Mayer, Mechanically controllable break junctions for molecular electronics. Adv. Mat. **25**, 4845–4867 (2013)
7. T. Konishi, M. Kiguchi, M. Takase, F. Nagasawa, H. Nabika, K. Ikeda, K. Uosaki, K. Ueno, H. Misawa, K. Murakoshi, Single molecule dynamics at a mechanically controllable break junction in solution at room temperature. J. Am. Chem. Soc. **135**, 1009–1014 (2013)
8. E. Lörtscher, J.W. Ciszek, J. Tour, H. Riel, Reversible and controllable switching of a single-molecule junction. Small **2**, 973–977 (2006)
9. C. Jia, B. Ma, N. Xin, X. Guo, Carbon electrode-molecule junctions: a reliable platform for molecular electronics. Acc. Chem. Res. **48**, 2565–2575 (2015)
10. Y. Zhao, M. Gobbi, L.E. Hueso, P. Samorì, Molecular approach to engineer two-dimensional devices for CMOS and beyond-CMOS applications. Chem. Rev. **122**, 50–131 (2022)
11. Y. Li, C. Yang, X. Guo, Single-molecule electrical detection: a promising route toward the fundamental limits of chemistry and life science. Acc. Chem. Res. **53**, 159–169 (2020)
12. W. Jeong, K. Kim, Y. Kim, W. Lee, P. Reddy, Characterization of nanoscale temperature fields during electromigration of nanowires. Sci. Rep. **4**, 1–6 (2014)
13. L.H. Yu, D. Natelson, The Kondo effect in C60 single-molecule transistors. Nano Lett. **4**, 79–83 (2004)
14. A.W. Ghosh, T. Rakshit, S. Datta, Gating of a molecular transistor: electrostatic and conformational. Nano Lett. **4**, 565–568 (2004)
15. M. Kalla, N.R. Chebrolu, A. Chatterjee, Quantum transport in a single molecular transistor at finite temperature. Sci. Rep. **11**, 1–14 (2021)
16. C.J. Lambert, Basic concepts of quantum interference and electron transport in single-molecule electronics. Chem. Soc. Rev. **44**, 875–888 (2015)
17. C.R. Arroyo, R. Frisenda, K. Moth-Poulsen, J.S. Seldenthuis, T. Bjørnholm, H.S.J. van der Zant, Quantum interference effects at room temperature in OPV-based single-molecule junctions. Nano. Res. Lett. **8**, 1–6 (2013)
18. P. Gehring, J.M. Thijssen, H.S.J. van der Zant, Single-molecule quantum-transport phenomena in break junctions. Nat. Rev. Phys. **1**, 381–396 (2019)
19. J. de Bruijckere, P. Gehring, M. Palacios-Corella, M. Clemente-León, E. Coronado, J. Paaske, P. Hedegård, H.S.J. van der Zant, Ground-state spin blockade in a single-molecule junction. Phys. Rev. Lett. **122**, 197701 (2019)

20. J.R. Widawsky, P. Darancet, J.B. Neaton, L. Venkataraman, Simultaneous determination of conductance and thermopower of single molecule junctions. Nano Lett. **12**, 354–358 (2012)
21. C. Bruot, J.L. Palma, L. Xiang, V. Mujica, M.A. Ratner, N. Tao, Piezoresistivity in single DNA molecules. Nat. Commun. **6**, 1–8 (2015)
22. M. Tsutsui, K. Matsubara, T. Ohshiro, M. Furuhashi, M. Taniguchi, T. Kawai, Electrical detection of single methylcytosines in a DNA oligomer. J. Am. Chem. Soc. **133**, 9124–9128 (2011)
23. S. Liu, X. Zhang, W. Luo, Z. Wang, X. Guo, M.L. Steigerwald, X. Fang, Single-molecule detection of proteins using aptamer-functionalized molecular electronic devices. Angew. Chem. Int. Ed. **50**, 2496–2502 (2011)
24. H. Reddy, K. Wang, Z. Kudyshev, L. Zhu, S. Yan, A. Vezzoli, S.J. Higgins, V. Gavini, A. Boltasseva, P. Reddy, V.M. Shalaev, E. Meyhofer, Determining plasmonic hot-carrier energy distributions via single-molecule transport measurements. Science **369**, 423–426 (2020)
25. A.N. Pal, D. Li, S. Sarkar, S. Chakrabarti, A. Vilan, L. Kronik, A. Smogunov, O. Tal, Nonmagnetic single-molecule spin-filter based on quantum interference. Nat. Commun. **10**, 1 (2019)
26. M. Ormaza, P. Abufager, B. Verlhac, N. Bachellier, M.L. Bocquet, N. Lorente, L. Limot, Controlled spin switching in a metallocene molecular junction. Nat. Commun. **8**, 1 (2017)
27. G. Ke, C. Duan, F. Huang, X. Guo, Electrical and spin switches in single-molecule junctions. InfoMat. **2**, 92–112 (2020)
28. I.V. Pobelov, G. Mészáros, K. Yoshida, A. Mishchenko, M. Gulcur, M.R. Bryce, T. Wandlowski, An approach to measure electromechanical properties of atomic and molecular junctions. J. Phys.: Condens. Matter. **24**, 164210 (2012)
29. B.Q. Xu, X.L. Li, X.Y. Xiao, H. Sakaguchi, N.J. Tao, Electromechanical and conductance switching properties of single oligothiophene molecules. Nano Lett. **5**, 1491–1495 (2005)
30. I. Diez-Perez, J. Hihath, T. Hines, Z.S. Wang, G. Zhou, K. Müllen, N. Tao, Controlling single-molecule conductance through lateral coupling of π orbitals. Nat. Nanotechnol. **6**, 226–231 (2011)
31. W. Chen, H. Li, J.R. Widawsky, C. Appayee, L. Venkataraman, R. Breslow, Aromaticity decreases single-molecule junction conductance. J. Am. Chem. Soc. **136**, 918–920 (2014)
32. X. Huang, C. Tang, J. Li, L.C. Chen, J. Zheng, P. Zhang, J. Le, R. Li, X. Li, J. Liu, Y. Yang, J. Shi, Z. Chen, M. Bai, H.L. Zhang, H. Xia, J. Cheng, Z.Q. Tian, W. Hong, Electric field-induced selective catalysis of single-molecule reaction. Sci. Adv. **5**, 3072–3093 (2019)
33. X. Xie, P. Li, Y. Xu, L. Zhou, Y. Yan, L. Xie, C. Jia, X. Guo, Single-molecule junction: a reliable platform for monitoring molecular physical and chemical processes. ACS Nano **16**, 3476–3505 (2022)
34. L. Xiang, J.L. Palma, Y. Li, V. Mujica, M.A. Ratner, N. Tao, Gate-controlled conductance switching in DNA. Nat. Commun. **8**, 1–10 (2017)
35. L. Meng, N. Xin, C. Hu, H. Sabea, M. Zhang, H. Jiang, Y. Ji, C. Jia, Z. Yan, Q. Zhang, L. Gu, X. He, P. Selvanathan, L. Norel, S. Rigaut, H. Guo, S. Meng, X. Guo, Dual-gated single-molecule field-effect transistors beyond Moore's law. Nat. Commun. **2022**(13), 1–6 (2022)
36. Z. Zhao, C. Guo, L. Ni, X. Zhao, S. Zhang, D. Xiang, In situ photoconductivity measurements of imidazole in optical fiber break-junctions. Nanoscale Horiz. **6**, 386–392 (2021)
37. Y. Kim, T.J. Hellmuth, D. Sysoiev, F. Pauly, T. Pietsch, J. Wolf, A. Erbe, T. Huhn, U. Groth, U.E. Steiner, E. Scheer, Charge transport characteristics of diarylethene photoswitching single-molecule junctions. Nano Lett. **12**, 3736–3742 (2012)
38. C. Tang, M. Shiri, H. Zhang, R.T. Ayinla, K. Wang, Light-driven charge transport and optical sensing in molecular junctions. J. Nanomater. **12**, 698 (2022)
39. C. Iacovita, M.V. Rastei, B.W. Heinrich, T. Brumme, J. Kortus, L. Limot, J.P. Bucher, Visualizing the spin of individual cobalt-phthalocyanine molecules. Phys. Rev. Lett. **101**, 116602 (2008)
40. C. Mathonière, H.J. Lin, D. Siretanu, R. Clérac, J.M. Smith, Photoinduced single-molecule magnet properties in a four-coordinate iron(II) spin crossover complex. J. Am. Chem. Soc. **135**, 19083–19086 (2013)
41. T. Miyamachi, M. Gruber, V. Davesne, M. Bowen, S. Boukari, L. Joly, F. Scheurer, G. Rogez, T.K. Yamada, P. Ohresser, E. Beaurepaire, W. Wulfhekel, Robust spin crossover and memristance across a single molecule. Nat. Commun. **3**, 1–6 (2012)
42. T.A. Su, H. Li, M.L. Steigerwald, L. Venkataraman, C. Nuckolls, Stereoelectronic switching in single-molecule junctions. Nat. Chem. **7**, 215–220 (2015)
43. F. Jiang, D.I. Trupp, N. Algethami, H. Zheng, W. He, A. Alqorashi, C. Zhu, C. Tang, R. Li, J. Liu, H. Sadeghi, J. Shi, R. Davidson, M. Korb, A.N. Sobolev, M. Naher, S. Sangtarash, P.J. Low, W. Hong, C.J. Lambert, Turning the tap: conformational control of quantum interference to modulate single-molecule conductance. Angew. Chem. Int. Ed. **58**, 18987–18993 (2019)
44. N. Darwish, A.C. Aragonès, T. Darwish, S. Ciampi, I. Díez-Pérez, Multi-responsive photo- and chemo-electrical single-molecule switches. Nano Lett. **14**, 7064–7070 (2014)
45. C. Jia, A. Migliore, N. Xin, S. Huang, J. Wang, Q. Yang, S. Wang, H. Chen, D. Wang, B. Feng, Z. Liu, G. Zhang, D.H. Qu, H. Tian, M.A. Ratner, H.Q. Xu, A. Nitzan, X. Guo, Covalently bonded single-molecule junctions with stable and reversible photoswitched conductivity. Science **352**, 1443–1445 (2016)
46. L. Yuan, N. Nerngchamnong, L. Cao, H. Hamoudi, E. del Barco, M. Roemer, R.K. Sriramula, D. Thompson, C.A. Nijhuis, Controlling the direction of rectification in a molecular diode. Nat. Commun. **6**, 1–11 (2015)
47. Z. Li, H. Li, S. Chen, T. Froehlich, C. Yi, C. Schönenberger, M. Calame, S. Decurtins, S.X. Liu, E. Borguet, Regulating a benzodifuran single molecule redox switch via electrochemical gating and optimization of molecule/electrode coupling. J. Am. Chem. Soc. **136**, 8867–8870 (2014)
48. G.D. Harzmann, R. Frisenda, H.S.J. van der Zant, M. Mayor, Single-molecule spin switch based on voltage-triggered distortion of the coordination sphere. Angew. Chem. Int. Ed. **54**, 13425–13430 (2015)
49. A.C. Aragonès, D. Aravena, J.I. Cerdá, Z. Acís-Castillo, H. Li, J.A. Real, F. Sanz, J. Hihath, E. Ruiz, I. Díez-Pérez, Large conductance switching in a single-molecule device through room temperature spin-dependent transport. Nano Lett. **16**, 218–226 (2016)
50. A. Vezzoli, Mechanoresistive single-molecule junctions. Nanoscale **14**, 2874–2884 (2022)
51. J.S. Meisner, M. Kamenetska, M. Krikorian, M.L. Steigerwald, L. Venkataraman, C. Nuckolls, A single-molecule potentiometer. Nano Lett. **11**, 1575–1579 (2011)
52. N. Xin, J. Wang, C. Jia, Z. Liu, X. Zhang, C. Yu, M. Li, S. Wang, Y. Gong, H. Sun, G. Zhang, Z. Liu, G. Zhang, J. Liao, D. Zhang, X. Guo, Stereoelectronic effect-induced conductance switching in aromatic chain single-molecule junctions. Nano Lett. **17**, 856–861 (2017)
53. A.K. Ismael, K. Wang, A. Vezzoli, M.K. Al-Khaykanee, H.E. Gallagher, I.M. Grace, C.J. Lambert, B. Xu, R.J. Nichols, S.J. Higgins, Side-group-mediated mechanical conductance switching in molecular junctions. Angew. Chem. Int. Ed. **56**, 15378–15382 (2017)
54. C. Wu, D. Bates, S. Sangtarash, N. Ferri, A. Thomas, S.J. Higgins, C.M. Robertson, R.J. Nichols, H. Sadeghi, A. Vezzoli, Folding a single-molecule junction. Nano Lett. **16**, 51 (2020)
55. S.Y. Quek, M. Kamenetska, M.L. Steigerwald, H.J. Choi, S.G. Louie, M.S. Hybertsen, J.B. Neaton, L. Venkataraman, Mechanically controlled binary conductance switching of a single-molecule junction. Nat Nanotechnol. **4**, 230–234 (2009)
56. R. Ramachandran, H.B. Li, W.Y. Lo, A. Neshchadin, L. Yu, J. Hihath, An electromechanical approach to understanding binding configurations in single-molecule devices. Nano Lett. **18**, 6638–6644 (2018)
57. T.A. Su, H. Li, V. Zhang, M. Neupane, A. Batra, R.S. Klausen, B. Kumar, M.L. Steigerwald, L. Venkataraman, C. Nuckolls, Single-molecule conductance in atomically precise germanium wires. J. Am. Chem. Soc. **137**, 12400–12405 (2015)
58. L. Gerhard, K. Edelmann, J. Homberg, M. Valášek, S.G. Bahoosh, M. Lukas, F. Pauly, M. Mayor, W. Wulfhekel, An electrically actuated molecular toggle switch. Nat. Commun. **8**, 1–10 (2017)
59. D. Stefani, K.J. Weiland, M. Skripnik, C. Hsu, M.L. Perrin, M. Mayor, F. Pauly, H.S.J. van der Zant, Large conductance variations in a mechanosensitive single-molecule junction. Nano Lett. **18**, 5981–5988 (2018)
60. J. Li, P. Shen, S. Zhen, C. Tang, Y. Ye, D. Zhou, W. Hong, Z. Zhao, B.Z. Tang, Mechanical single-molecule potentiometers with large switching factors from ortho-pentaphenylene foldamers. Nat. Commun. **12**, 1–11 (2021)
61. M. Camarasa-Gómez, D. Hernangómez-Pérez, M.S. Inkpen, G. Lovat, E.D. Fung, X. Roy, L. Venkataraman, F. Evers, Mechanically tunable quantum

interference in ferrocene-based single-molecule junctions. Nano Lett. **20**, 6381–6386 (2020)
62. L.Q. Pei, J.R. Horsley, J.W. Seng, X. Liu, Y.Q. Yeoh, M.X. Yu, X.H. Wu, A.D. Abell, J.F. Zheng, X.S. Zhou, J. Yu, S. Jin, Mechanically induced switching between two discrete conductance states: a potential single-molecule variable resistor. ACS Appl. Mater. Interfaces. **13**, 57646–57653 (2021)
63. W. Haiss, T. Albrecht, H. van Zalinge, S.J. Higgins, D. Bethell, H. Höbenreich, D.J. Schiffrin, R.J. Nichols, A.M. Kuznetsov, J. Zhang, Q. Chi, J. Ulstrup, Single-molecule conductance of redox molecules in electrochemical scanning tunneling microscopy. J. Phys. Chem. B. **111**, 6703–6712 (2007)
64. Y. Li, M. Baghernejad, A.G. Qusiy, D. Zsolt Manrique, G. Zhang, J. Hamill, Y. Fu, P. Broekmann, W. Hong, T. Wandlowski, D. Zhang, C. Lambert, Three-state single-molecule naphthalenediimide switch: integration of a pendant redox unit for conductance tuning. Angew. Chem. Int. Ed. **54**, 13586–13589 (2015)
65. F. Schwarz, G. Kastlunger, F. Lissel, C. Egler-Lucas, S.N. Semenov, K. Venkatesan, H. Berke, R. Stadler, E. Lörtscher, Field-induced conductance switching by charge-state alternation in organometallic single-molecule junctions. Nat. Nanotechnol. **11**, 170–176 (2015)
66. M. Baghernejad, D. Zsolt Manrique, C. Li, T. Pope, U. Zhumaev, I. Pobelov, P. Moreno-García, V. Kaliginedi, C. Huang, W. Hong, C. Lambert, T. Wandlowski, Highly-effective gating of single-molecule junctions: an electrochemical approach. Chem. Commun. **50**, 15975–15978 (2014)
67. N.J. Kay, S.J. Higgins, J.O. Jeppesen, E. Leary, J. Lycoops, J. Ulstrup, R.J. Nichols, Single-molecule electrochemical gating in ionic liquids. J. Am. Chem. Soc. **134**, 16817–16826 (2012)
68. S. Guo, J.M. Artés, I. Díez-Pérez, Electrochemically-gated single-molecule electrical devices. Electrochim. Acta. **110**, 741–753 (2013)
69. J. Li, S. Pudar, H. Yu, S. Li, J.S. Moore, J. Rodríguez-López, N.E. Jackson, C.M. Schroeder, Reversible switching of molecular conductance in viologens is controlled by the electrochemical environment. J. Phys. Chem. C. **125**, 21862–21872 (2021)
70. Y. Li, H. Wang, Z. Wang, Y. Qiao, J. Ulstrup, H.Y. Chen, G. Zhou, N. Tao, Transition from stochastic events to deterministic ensemble average in electron transfer reactions revealed by single-molecule conductance measurement. Proc. Natl. Acad. Sci. **116**, 3407–3412 (2019)
71. M. Koole, J.M. Thijssen, H. Valkenier, J.C. Hummelen, H.S.J.V. der Zant, Electric-field control of interfering transport pathways in a single-molecule anthraquinone transistor. Nano Lett. **15**, 5569–5573 (2015)
72. Z. Li, M. Smeu, A. Rives, V. Maraval, R. Chauvin, M.A. Ratner, E. Borguet, Towards graphyne molecular electronics. Nat. Commun. **6**, 1–9 (2015)
73. C. Wu, X. Qiao, C.M. Robertson, S.J. Higgins, C. Cai, R.J. Nichols, A. Vezzoli, A chemically soldered polyoxometalate single-molecule transistor. Angew. Chem. Int. Ed. **59**, 12029–12034 (2020)
74. S. Naghibi, S. Sangtarash, V.J. Kumar, J.Z. Wu, M.M. Judd, X. Qiao, E. Gorenskaia, S.J. Higgins, N. Cox, R.J. Nichols, H. Sadeghi, P.J. Low, A. Vezzoli, Redox-addressable single-molecule junctions incorporating a persistent organic radical. Angew. Chem. Int. Ed. **61**, e202116985 (2022)
75. X. Yin, Y. Zang, L. Zhu, J.Z. Low, Z.F. Liu, J. Cui, J.B. Neaton, L. Venkataraman, L.M. Campos, A reversible single-molecule switch based on activated antiaromaticity. Sci. Adv. **3**, 1 (2017)
76. N. Tallarida, L. Rios, V.A. Apkarian, J. Lee, Isomerization of one molecule observed through tip-enhanced Raman spectroscopy. Nano Lett. **15**, 6386–6394 (2015)
77. C. Huang, M. Jevric, A. Borges, S.T. Olsen, J.M. Hamill, J.T. Zheng, Y. Yang, A. Rudnev, M. Baghernejad, P. Broekmann, A.U. Petersen, T. Wandlowski, K.V. Mikkelsen, G.C. Solomon, M. Brøndsted Nielsen, W. Hong, Single-molecule detection of dihydroazulene photo-thermal reaction using break junction technique. Nat. Commun. **8**, 1–7 (2017)
78. M. Gobbi, S. Bonacchi, J.X. Lian, A. Vercouter, S. Bertolazzi, B. Zyska, M. Timpel, R. Tatti, Y. Olivier, S. Hecht, M.V. Nardi, D. Beljonne, E. Orgiu, P. Samorì, Collective molecular switching in hybrid superlattices for light-modulated two-dimensional electronics. Nat. Commun. **9**, 1–9 (2018)
79. R. Klajn, Spiropyran-based dynamic materials. Chem. Soc. Rev. **43**, 148–184 (2013)
80. E.S. Tam, J.J. Parks, W.W. Shum, Y.W. Zhong, M.B. Santiago-Berríos, X. Zheng, W. Yang, G.K.L. Chan, H.D. Abruña, D.C. Ralph, Single-molecule conductance of pyridine-terminated dithienylethene switch molecules. ACS Nano **5**, 5115–5123 (2011)
81. T. Kudernac, N. Katsonis, W.R. Browne, B.L. Feringa, Nano-electronic switches: light-induced switching of the conductance of molecular systems. J. Mater. Chem. **19**, 7168–7177 (2009)
82. X. Huang, T. Li, Recent progress in the development of molecular-scale electronics based on photoswitchable molecules. J. Mater. Chem. C. **8**, 821–848 (2020)
83. L. Meng, N. Xin, C. Hu, J. Wang, B. Gui, J. Shi, C. Wang, C. Shen, G. Zhang, H. Guo, S. Meng, X. Guo, Side-group chemical gating via reversible optical and electric control in a single molecule transistor. Nat. Commun. **10**, 1–8 (2019)
84. X. Xiao, B. Xu, N. Tao, Conductance titration of single-peptide molecules. J Am Chem Soc. **126**, 5370–5371 (2004)
85. L. Li, W.Y. Lo, Z. Cai, N. Zhang, L. Yu, Proton-triggered switch based on a molecular transistor with edge-on gate. Chem. Sci. **7**, 3137–3141 (2016)
86. J.T.C. Wojtyk, A. Wasey, N.N. Xiao, P.M. Kazmaier, S. Hoz, C. Yu, R.P. Lemieux, E. Buncel, Elucidating the mechanisms of acidochromic spiropyran-merocyanine interconversion. J. Phys. Chem. A. **111**, 2511–2516 (2007)
87. X. Guo, J.P. Small, J.E. Klare, Y. Wang, M.S. Purewal, I.W. Tam, B.H. Hong, R. Caldwell, L. Huang, S. O'Brien, J. Yan, R. Breslow, S.J. Wind, J. Hone, P. Kim, C. Nuckolls, Covalently bridging-gaps in single-walled carbon nanotubes with conducting molecules. Science **311**, 356–359 (2006)
88. C.P. Tao, C.C. Jiang, Y.H. Wang, J.F. Zheng, Y. Shao, X.S. Zhou, Single-molecule sensing of interfacial acid-base chemistry. J. Phys. Chem. Lett. **11**, 10023–10028 (2020)
89. Z. Li, M. Smeu, S. Afsari, Y. Xing, M.A. Ratner, E. Borguet, Single-molecule sensing of environmental pH—an STM break junction and NEGF-DFT approach. Angew. Chem. Int. Ed. **53**, 1098–1102 (2014)
90. R.J. Brooke, D.S. Szumski, A. Vezzoli, S.J. Higgins, R.J. Nichols, W. Schwarzacher, Dual control of molecular conductance through ph and potential in single-molecule devices. Nano Lett. **18**, 1317–1322 (2018)
91. G. Yang, S. Sangtarash, Z. Liu, X. Li, H. Sadeghi, Z. Tan, R. Li, J. Zheng, X. Dong, J. Liu, Y. Yang, J. Shi, Z. Xiao, G. Zhang, C. Lambert, W. Hong, D. Zhang, Protonation tuning of quantum interference in azulene-type single-molecule junctions. Chem. Sci. **8**, 7505–7509 (2017)
92. Y.P. Zhang, L.C. Chen, Z.Q. Zhang, J.J. Cao, C. Tang, J. Liu, L.L. Duan, Y. Huo, X. Shao, W. Hong, H.L. Zhang, Distinguishing diketopyrrolopyrrole isomers in single-molecule junctions via reversible stimuli-responsive quantum interference. J. Am. Chem. Soc. **140**, 6531–6535 (2018)
93. J. Martínez-Blanco, C. Nacci, S.C. Erwin, K. Kanisawa, E. Locane, M. Thomas, F. von Oppen, P.W. Brouwer, S. Fölsch, Gating a single-molecule transistor with individual atoms. Nat. Phys. **11**, 640–644 (2015)
94. Y. Li, M. Buerkle, G. Li, A. Rostamian, H. Wang, Z. Wang, D.R. Bowler, T. Miyazaki, L. Xiang, Y. Asai, G. Zhou, N. Tao, Gate controlling of quantum interference and direct observation of anti-resonances in single molecule charge transport. Nat. Mater. **18**, 357–363 (2019)
95. H. Song, Y. Kim, Y.H. Jang, H. Jeong, M.A. Reed, T. Lee, Observation of molecular orbital gating. Nature **462**, 1039–1043 (2009)
96. Y. Kim, W. Jeong, K. Kim, W. Lee, P. Reddy, Electrostatic control of thermoelectricity in molecular junctions. Nat. Nanotechnol. **9**, 881–885 (2014)
97. N. Xin, J. Guan, C. Zhou, X. Chen, C. Gu, Y. Li, M.A. Ratner, A. Nitzan, J.F. Stoddart, X. Guo, Concepts in the design and engineering of single-molecule electronic devices. Nat. Rev. Phys. **1**, 211–230 (2019)
98. J. Bai, X. Li, Z. Zhu, Y. Zheng, W. Hong, J. Bai, X. Li, Z. Zhu, Y. Zheng, W. Hong, Single-molecule electrochemical transistors. Adv. Mater. **33**, 2005883 (2021)
99. J. Liu, X. Huang, F. Wang, W. Hong, Quantum interference effects in charge transport through single-molecule junctions: detection, manipulation, and application. Acc. Chem. Res. **52**, 151–160 (2019)
100. B. Capozzi, Q. Chen, P. Darancet, M. Kotiuga, M. Buzzeo, J.B. Neaton, C. Nuckolls, L. Venkataraman, Tunable charge transport in single-molecule junctions via electrolytic gating. Nano Lett. **14**, 1400–1404 (2014)
101. J. Bai, A. Daaoub, S. Sangtarash, X. Li, Y. Tang, Q. Zou, H. Sadeghi, S. Liu, X. Huang, Z. Tan, J. Liu, Y. Yang, J. Shi, G. Mészáros, W. Chen, C. Lambert, W. Hong, Anti-resonance features of destructive quantum interference in single-molecule thiophene junctions achieved by electrochemical gating. Nat. Mater. **18**, 364–369 (2019)

102. Y.H. Wang, F. Yan, D.F. Li, Y.F. Xi, R. Cao, J.F. Zheng, Y. Shao, S. Jin, J.Z. Chen, X.S. Zhou, Enhanced gating performance of single-molecule conductance by heterocyclic molecules. J. Phys. Chem. Lett. **12**, 758–763 (2021)
103. J.E. Greenwald, J. Cameron, N.J. Findlay, T. Fu, S. Gunasekaran, P.J. Skabara, L. Venkataraman, Highly nonlinear transport across single-molecule junctions via destructive quantum interference. Nat. Nanotechnol. **16**, 313–317 (2020)
104. J. Sinova, I. Žutić, New moves of the spintronics tango. Nat. Mater. **11**, 368–371 (2012)
105. S. Wagner, F. Kisslinger, S. Ballmann, F. Schramm, R. Chandrasekar, T. Bodenstein, O. Fuhr, D. Secker, K. Fink, M. Ruben, H.B. Weber, Switching of a coupled spin pair in a single-molecule junction. Nat. Nanotechnol. **8**, 575–579 (2013)
106. T. Stuyver, M. Perrin, P. Geerlings, F. de Proft, M. Alonso, Conductance switching in expanded porphyrins through aromaticity and topology changes. J. Am. Chem. Soc. **140**, 1313–1326 (2018)
107. K. Wang, A. Vezzoli, I.M. Grace, M. McLaughlin, R.J. Nichols, B. Xu, C.J. Lambert, S.J. Higgins, Charge transfer complexation boosts molecular conductance through Fermi level pinning. Chem. Sci. **10**, 2396–2403 (2019)
108. G. Grynova, C. Corminboeuf, Topology-driven single-molecule conductance of carbon nanothreads. J. Phy. Chem. Lett. **10**, 825–830 (2019)
109. J.H. Tang, Y. Li, Q. Wu, Z. Wang, S. Hou, K. Tang, Y. Sun, H. Wang, H. Wang, C. Lu, X. Wang, X. Li, D. Wang, J. Yao, C.J. Lambert, N. Tao, Y.W. Zhong, P.J. Stang, Single-molecule level control of host-guest interactions in metallocycle-C60 complexes. Nat. Commun. **10**, 1–9 (2019)
110. A.P. Ivanov, E. Instuli, C.M. McGilvery, G. Baldwin, D.W. McComb, T. Albrecht, J.B. Edel, DNA tunneling detector embedded in a nanopore. Nano Lett. **11**, 279–285 (2011)
111. A. Fanget, F. Traversi, S. Khlybov, P. Granjon, A. Magrez, L. Forró, A. Radenovic, Nanopore integrated nanogaps for DNA detection. Nano Lett. **14**, 244–249 (2014)
112. M. di Ventra, M. Taniguchi, Decoding DNA, RNA and peptides with quantum tunnelling. Nat. Nanotechnol. **11**, 117–126 (2016)
113. Y. Zhang, Q.S. Meng, L. Zhang, Y. Luo, Y.J. Yu, B. Yang, Y. Zhang, R. Esteban, J. Aizpurua, Y. Luo, J.L. Yang, Z.C. Dong, J.G. Hou, Sub-nanometre control of the coherent interaction between a single molecule and a plasmonic nanocavity. Nat. Commun. **8**, 1–7 (2017)