ing "chip" that enables cells to generate vast, combinatorially complex arrays of communication pathways.

References and Notes

1. A. Saiardi, R. Bhandari, A. C. Resnick, A. M. Snowman, S. H. Snyder, *Science* **306**, 2101 (2004).
2. G. N. Europe-Finner *et al.*, *Biochem. Biophys. Res. Commun.* **181**, 191 (1991).
3. F. S. Menniti *et al.*, *J. Biol. Chem.* **268**, 3850 (1993).
4. L. Stephens *et al.*, *J. Biol. Chem.* **268**, 4009 (1993).
5. A. Saiardi *et al.*, *Curr. Biol.* **9**, 1323 (1999).
6. J. D. York *et al.*, *Science* **285**, 96 (1999).
7. J. D. York, in *Handbook of Cell Signaling*, R. A. Bradshaw, E. Dennis, Eds. (Academic Press, New York, 2003), pp. 229–232.
8. S. B. Shears, *Biochem. J.* **377**, 265 (2004).
9. A. Saiardi *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 14206 (2002).
10. H. R. Luo *et al.*, *Biochemistry* **41**, 2509 (2002).
11. H. R. Luo *et al.*, *Cell* **114**, 559 (2003).
12. S. J. York *et al.*, *J. Biol. Chem.*, published online 23 November 2004 (10.1074/jbc.M412070200).
13. X. Pesesse *et al.*, *J. Biol. Chem.* **279**, 43378 (2004).
14. R. F. Irvine, M. J. Schell, *Nature Rev. Mol. Cell Biol.* **2**, 327 (2001).
15. S. H. Snyder, personal communication.
16. B. W. Agranoff, *Trends Biochem. Sci.* **3**, N283 (1978).
17. We thank S. Shears for helpful comments and the Snyder laboratory for sharing unpublished information.

10.1126/science.1107225

CHEMISTRY

Whence Molecular Electronics?

Amar H. Flood, J. Fraser Stoddart, David W. Steuerman, James R. Heath

The drive toward yet further miniaturization of silicon-based electronics has led to a revival of efforts to build devices with molecular-scale components. The field of molecular electronics is teeming with results, rationalizations, and speculations. Some claims may have been exaggerated, but news stories of a crisis in the field (*1*) are premature. Reports of passive molecular electronics devices, such as tunnel junctions and rectifiers, as well as of active devices, for example, single-molecule transistors and molecular switch tunnel junctions, have withstood scientific scrutiny. Simple molecular electronic devices usually consist of organic molecules sandwiched between conducting electrodes. According to early predictions, such devices could show electron tunneling (*2*) or one-way flow of current (rectification) through the molecule (*3*). In most tunneling junctions, linear alkanes are sandwiched between metal electrodes. Measurements over the past 25 years (*4*, *5*) have largely validated McConnell's prediction (*2*) that the tunnel current depends exponentially on the length of the molecules between conducting electrodes. In rectifiers, a molecule composed of an electron donor, a bridge, and an electron acceptor is extended between two electrodes (see the first figure, top panel). Experiments (*6*, *7*) have again validated the early prediction by Aviram and Ratner (*3*).

Enhanced online at www.sciencemag.org/cgi/content/full/306/5704/2055

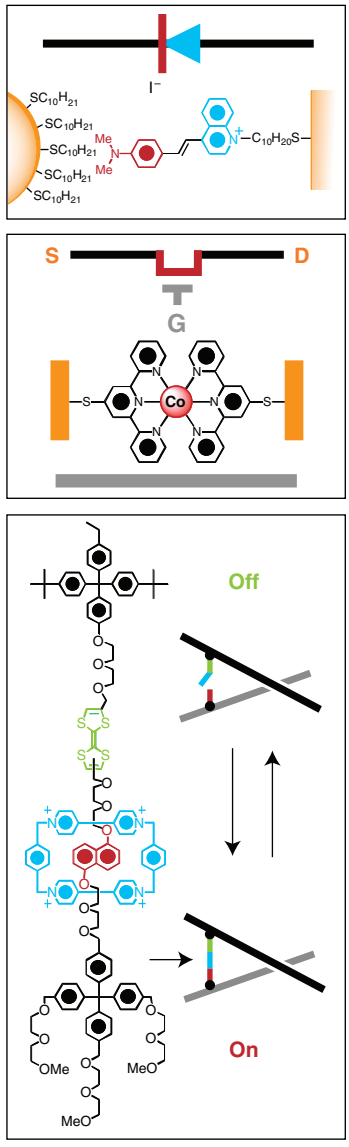
A. H. Flood and J. F. Stoddart are at the California NanoSystems Institute and the Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095, USA. E-mail: amarf@chem.ucla.edu, stoddart@chem.ucla.edu D. W. Steuerman is in the Department of Physics, University of California, Santa Barbara, CA 93106, USA. E-mail: dws@physics.ucsb.edu J. R. Heath is in the Division of Chemistry and Chemical Engineering, California Institute of Technology, CA 91125, USA. E-mail: heath@caltech.edu

However, for both types of devices, the devil has been in the details, and reaching agreement between experiments and theory has not been straightforward. In the case of tunnel junctions, McConnell's prediction breaks down for alkanes with more than about 16 carbon atoms in the chain, because coherent tunneling is replaced by diffusive charge transport in longer chains. Furthermore, in all devices, the molecules tilt at an angle smaller than 90° with respect to the electrode surfaces. This angle—and hence the separation between the electrodes—varies across different device constructions. Such variations can affect the measured current levels and can also dictate at which alkane chain length diffusive transport replaces tunneling. Other issues, such as the choice of electrode materials, can have similar effects.

In the case of rectifiers, it has turned out to be relatively easy to observe rectification, but nontrivial to observe true molecular rectification. This problem arises because current can be rectified in many parts of the device—for example, at the molecule/electrode interfaces. True molecular rectification is observed only if the donor–bridge–acceptor component of the molecule is extended between the electrodes, and for only a relatively small range of donor and acceptor molecular orbital energy levels. Thus, strict attention to the molecular components, and to the molecule/electrode interfaces, is required.

Active molecular electronic devices include single-molecule transistors and molecular switch tunnel junctions. The development of these more complex devices has been guided by experiment rather than theory. To date, only a couple of systems have passed scientific scrutiny from multiple laboratories. To validate such devices, one compelling approach has been to identify unique properties that can be observed and quantified in both the devices and in solution.

In a single-molecule transistor, a molecule is bridged across a 1- to 4-nm-wide electrode gap (see the first figure, middle panel). Three-terminal devices of this kind are powerful tools for exploring the fundamental physics of molecular devices: Parameters such as temperature, and electric and magnetic fields, may all be varied while the spectroscopic response is measured. Using single-molecule

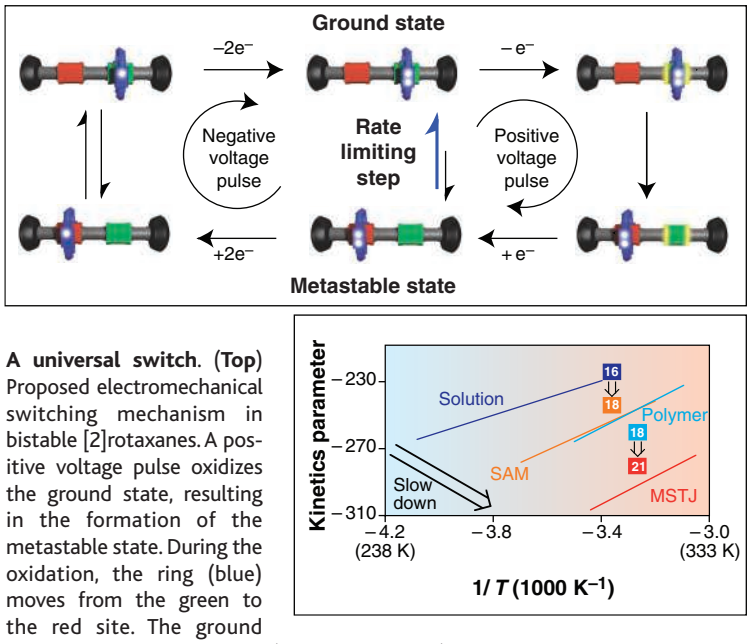


Molecular electronic devices. (Top) A molecular rectifier constructed from donor (red), bridge (black), and acceptor (blue) components. **(Middle)** A single-molecule transistor constructed from a symmetrical cobalt complex. S, source; D, drain; G, gate. **(Bottom)** A molecular switch tunnel junction in its Off and On states. (Left) Structural formula of the On state of a bistable [2]rotaxane.

Published by AAAS

transistors, two groups (*8*, *9*) have observed a unique type of quantum mechanical resonance, called a Kondo resonance, that can be correlated with a particular oxidation state—observed in solution-phase experiments—of the molecule.

Again, however, the devil is in the details. In particular, how the single-molecule transistors are made, the way in which molecules are assembled across the junctions, whether the molecules are bound covalently or noncovalently to the electrodes, and what electrode materials are used all play critical roles in either masking or revealing unique molecular electronic properties. Thus, despite early successes, it remains unclear whether single-molecule transistors can emerge as a general spectroscopic tool for guiding the development of molecular electronics.



A universal switch. (Top) Proposed electromechanical switching mechanism in bistable [2]rotaxanes. A positive voltage pulse oxidizes the ground state, resulting in the formation of the metastable state. During the oxidation, the ring (blue) moves from the green to the red site. The ground state is reformed thermally (rate-limiting step) or following a negative voltage pulse. A similar mechanism holds for bistable [2]catenanes (*13*). **(Bottom)** As shown in this Eyring plot, the kinetics of the rate-limiting step depend on the environment, reflecting a slowdown of the switching cycle as the free energy barrier increases from 16 to 21 kcal/mol. Environments: solution; self-assembled monolayer (SAM); polymer; molecular switch tunnel junction (MSTJ).

A second active device is a two-terminal molecular switch tunnel junction (see the first figure, bottom panel). The goal here is to design a molecule that, at a specific voltage, switches from a stable structure (isomer) to another, metastable isomer with a different conductivity and remains in the latter state until either another voltage pulse is applied or thermal fluctuations cause a return to the original isomer. The two states of the molecule correspond to the On and Off states of the switch, and the finite stability of the metastable state leads to a hysteretic current/voltage response that forms the basis of the switch. However, such switching behavior can also arise from the intrinsic device capacitance, from charge storage in defect sites at the molecule/electrode interface, or from electrochemical modification of the electrode materials (*10*). Such artifacts can be ruled out through careful control experiments, but some other, nonmolecular mechanism may nevertheless contribute to the switching response. Thus, the challenge is not just to rule out artifacts, but also to verify that the effect is molecular in origin by establishing a correlation to solution-phase observations.

We have previously reported (*11*) on molecular switch tunnel junctions that contain a monolayer of bistable mechanically interlocked molecules—such as the [2]rotaxane (*12*) shown in the lower panel of the first figure—sandwiched between silicon and metallic electrodes. These devices can be voltage-switched between a stable Off and a metastable On state. For the rotaxane case, we attributed these observations to an electrochemically driven translation (second figure, top panel) of the viologen-containing ring (colored blue) from the tetrathiafulvalene (green) site to the dioxynaphthalene (red) site to form the metastable state. The free energy barrier for relaxation back to the ground state provides an opportunity to correlate the device characteristics with molecular properties in solution.

To establish this correlation, we performed variable temperature electrochemical measurements (*13*) to quantify the metastable-to-ground state relaxation of these molecular switches not only in solution, but also in self-assembled monolayers and in polymer matrices, as well as in the molecular switch tunnel junctions. The free energy barriers to relaxation (see the second figure, bottom panel) of the switches in these four different environments are, respectively, 16, 18, 18, and 21 kcal mol^{-1} at room temperature. Thus, although the corresponding relaxation rates significantly slow down by a factor of 10,000 as the molecules are increasingly confined, the mechanism remains the same: It is universal.

Several other groups have reported theoretical (*14*) and experimental (*15*) studies on similar molecular mechanical systems in various environments. For example, Katz *et al.* have demonstrated a fuel cell in which a rotaxane self-assembled on gold electrode surfaces transports electrons from glucose oxidase to the electrode (*15*). The rotaxane bears a cyclophane that shuttles along the molecular string toward the electrode and back again within about 3 and 12 ms, respectively. Photo-driven relative movements (μs) of the components in a hydrogen-bonded rotaxane have been demonstrated (*16*). Poleschak *et al.* have shown that mechanical movements in bistable, copper-based catenanes and rotaxanes display (*17*) lifetimes of microseconds to hours depending on their structures. The structures of molecular switches can thus govern switching kinetics (*13*). This discovery augurs well for achieving a fundamental goal in the field: chemical control over the physical properties of electronic devices.

Molecular electronics will mature into a powerful technology only if its development is based on sound scientific conclusions that have been tried and tested at every step. Reaching these objectives requires a detailed understanding of the molecule/electrode interface, as well as developing methods for manufacturing reliable devices and ensuring their robustness. Although applications involving single devices already exist (*18*), the next-generation technologies will most likely consist of hybrid devices that combine molecular with existing electronics.

References

1. R. F. Service, *Science* **302**, 556 (2003).
2. H. McConnell, *J. Chem. Phys.* **35**, 508 (1961).
3. A. Aviram, M. A. Ratner, *Chem. Phys. Lett.* **29**, 277 (1974).
4. E. E. Polymeropoulos, J. Sagiv, *J. Chem. Phys.* **69**, 1836 (1978).
5. T. Lee *et al.*, *J. Phys. Chem. B* **108**, 8742 (2004).
6. R. M. Metzger, *Chem. Rev.* **103**, 3803 (2003).
7. G. J. Ashwell, W. D. Tyrrell, A. J. Whittam, *J. Am. Chem. Soc.* **126**, 7102 (2004).
8. J. Park *et al.*, *Nature* **417**, 722 (2002).
9. W. Liang, M. P. Shores, M. Bockrath, J. R. Long, H. Park, *Nature* **417**, 725 (2002).
10. C. N. Lau, D. R. Stewart, R. S. Williams, M. Bockrath, *Nano Lett.* **4**, 569 (2004).
11. C. P. Collier *et al.*, *Science* **289**, 1172 (2000).
12. Y. Luo *et al.*, *ChemPhysChem* **3**, 519 (2002).
13. A. H. Flood *et al.*, *Chem. Eur. J.* **10**, 6558 (2004).
14. Y. H. Jang, S. Hwang, Y.-H. Kim, S. S. Jang, W. A. Goddard III, *J. Am. Chem. Soc.* **126**, 12636 (2004).
15. E. Katz, O, Lioubashevski, I. Willner, *J. Am. Chem. Soc.*, **126**, 15520 (2004).
16. A. M. Brouwer *et al.*, *Science* **291**, 2124 (2001).
17. I. Poleschak, J.-M. Kern, J.-P. Sauvage, *Chem. Commun.* 474 (2004).
18. B. Feldman *et al.*, *Diabetes Technol. Ther.* **2**, 221 (2000).

10.1126/science.1106195

Published by AAAS