gible in normal skin but increases dramatically in skin treated with the carcinogen combination, and is even higher at sites where papillomas and carcinomas eventually form (*1*). Killing of Rae-1– and H60-positive skin cells by γδ IELs requires both NKG2d and γδ TCR, suggesting that engagement of NKG2d with its ligand provides the costimulatory signal to the TCR. It remains to be determined whether αβ IELs, which also express NKG2d, behave in a similar way to γδ IELs.

These results suggest that although the ligands for γδ TCR may be constitutively expressed, it is the inducible ligands for NKG2d that are the critical sensors of stress, costimulating IELs with the rapid kinetics characteristic of innate immunity (see the figure). The nature of the stress stimuli that induce the expression of NKG2d ligands has yet to be fully characterized. From the standpoint of tumor surveillance by the immune system, the relevant stressors—UV light in the case of skin, and gut-derived carcinogens in the case of intestinal epithelium—are both likely to be genotoxic (to damage the DNA of cells). Elucidating the stimuli and signals that induce expression of activating ligands for these different IEL populations will shed light on how regional immune networks protect specific epithelial tissues, our body's frontline defense against tumors and pathogens.

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PERSPECTIVES: MOLECULAR ELECTRONICS

It's All About Contacts

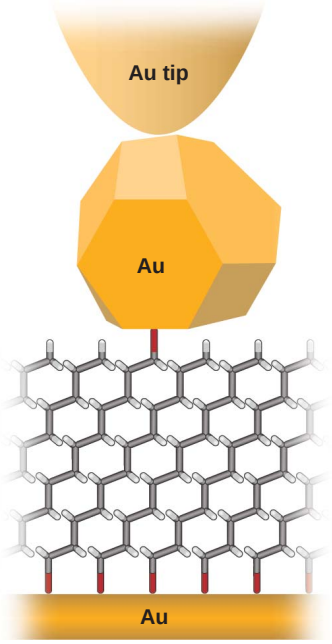
K. W. Hipps

The goal of building sophisticated electronic devices from individual molecules has spurred studies of single-molecule rectification (*1*), nanotube-based transistors (*2*), and negative differential resistance from small collections of molecules (*3*). The primary problems facing the molecular electronics designer are measuring and predicting electron transport. Molecular electronics will also require reliable molecular wires to carry signals from one molecular circuit element to another.

A key requirement in all these studies is the ability to measure the conductivity of a single molecule. To do so, we must connect a macroscopic current source and volt meter to each end of a single molecule. Molecular electronics is thus very much about contacts. Ideally, these contacts should be ohmic so that any nonlinearity in the conductivity of the wire can be correctly attributed and studied. They must also be low in resistance to ensure that the properties measured are those of the molecule and not those of the molecule-contact interface. Moreover, the medium surrounding and supporting the molecule must be several orders of magnitude more insulating than the molecule itself because the contact area of the support with the electrical contacts is often much greater than that between the electrical contacts and the molecule.

To see how hard it can be to determine the conductivity of an individual molecule, consider the case of DNA. Depending on the study, one finds that DNA is an insulator (*4*), semiconductor (*5*), conductor (*6*), or proximity-induced superconductor (*7*).

Dunlap *et al.* (*4*) used a scanning tunneling microscope to image DNA that was held, segment wise, onto a Pt/C-coated surface by patches of Pt/C overcoating. They were able to follow strands of λDNA between and through the coated segments. The uncoated regions had such high resistance that they appeared in negative contrast. The authors estimated a resistivity of 10^5 ohm-cm and concluded that DNA is a good insulator. However, this measurement was more about metal-DNA current injection and short-axis conductivity than about the commonly considered long-axis conductivity through π orbitals in adjacent base pairs.



Molecular solder? Cui *et al.*'s (*13*) experiment allows reliable measurements of molecular conductivity for a range of different molecules.

Porath *et al.* (*5*) studied conduction through a single, 10.4-nm-long, double-stranded DNA oligomer trapped between Pt electrodes. They observed wide band-gap semiconductor-like behavior. An unexpected result was the widening of the gap with increasing temperature. The authors state that the nature of the contact resistance between the metallic electrode and DNA is not well understood and suggest that there is no good metallic contact.

Fink and Schoenenberger (*6*) imaged λDNA ropes assumed to consist of a few double-stranded DNA molecules as they made electrical contact with a sharp tungsten probe. The DNA ropes were suspended across holes in a gold-coated carbon grid and imaged with a low-energy electron point source. A tungsten tip was then used to make contact with a rope and sever it, thereby producing a conduction path from the tip through the rope to the gold-coated grid. The authors estimate a resistivity of 1 milliohm-cm for a single DNA double strand and conclude that DNA is a conductor. The authors clearly have excellent mechanical contact between DNA and tip, but it is not clear that they have good electrical contact. Thus, their measurement is an upper limit for the resistivity. They solve the problem of stray parallel currents by keeping the strands in vacuum during the study.

Very recently, Kasumov *et al.* (*7*) have studied the conductivity of 16-μm-long strands of λDNA combed across a 0.5-μm gap between Re/C electrodes. Their measurements were on small sets of molecules (about 10) rather than a single molecule. The resistance per molecule was less than

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100 kiloohms, one order of magnitude smaller than that of (*6*), and varied only weakly with temperature. They attribute the lower resistivity to better molecule-electrode contacts. Moreover, for two of three samples, proximity-induced superconductivity was observed in their DNA strands.

These results are probably not the last chapter in this saga that is more about contacts than about molecular conduction. If simply making physical contact between a metal and a molecule is not enough to guarantee good electrical contact, what is?

When using scanning probe microscopy, pushing harder on the contact is not the answer. Generally, one of three things happens: The molecule moves under the contact (*8*), it is irreversibly deformed (*9*), or its electronic structure changes as a function of applied stress. In the first case, the tip and the molecule still interact through a tunneling barrier, but the barrier changes depending on which functional group in the molecule is moved closest to the tip by the applied pressure. The current thus changes with increased contact force but not necessarily in a way that reflects the molecular conductivity. In the second case, typical of large molecules with secondary structure, the sample is no longer what we started with and any results are irrelevant to the original molecule. The third case is best known for fullerenes (*10*).

It has long been recognized that to make good electrical contact between a molecule and a conducting substrate, a chemical bond is required. This is usually done with sulfur or selenium bound to gold or silver. Tour has called these connections "molecular alligator clips" (*11*). It is easy to take advantage of this concept at one electrode but much more difficult to do so at two. When a notched gold wire is broken in a solution of benzene-1,4-dithiol (a small molecule with alligator clips at both ends) and the ends are brought together until current flows, this results in a junction formed from a small number of molecules, most of which are chemically bonded to both electrodes (*12*). This break junction geometry gives relatively reproducible results when applied to small rigid molecules but is not easily adapted for longer and more flexible systems. Moreover, the high density of adjacent, singly connected molecules introduces concerns about stray parallel currents.

On page 571 of this issue, Cui *et al.* present a simple method for making good electrical contacts to variable length organic molecules (*13*). They use thiol groups to make well-defined chemical bonds to a gold base electrode and a gold nanoparticle top electrode. Contact to the nanoparticle is made through physical contact with a gold-coated atomic force microscopy tip. The molecule is thus covalently bonded to gold at both ends (see the figure). Isolation of the current to a single molecule is produced by diluting the dithiol functionalized alkane in a sea of monofunctionalized alkanes. Hence, even though the nanoparticle is much larger than the molecule of interest, the number of actual contacts per particle is small and peaks at a single contact per particle.

There are three especially exciting features of this work. The first is the statistical significance of the data. Unlike almost all previous reports, which rely on at most a handful of replications, Cui *et al*.'s report is based on more than 4000 separate measurements. Second, the computed current-voltage curves agree with experiment to within a factor of six, better than any previous work and with no adjustable parameters. Finally, the method can be extended to other nanoparticles and to functional groups other than thiol.

For the first time, it will be possible to systematically study the molecule-contact interface in a reliable and reproducible way. If molecular electronics is all about contacts, the work of Cui *et al*. finally gives us a tool to begin in earnest the study of single-molecule devices.

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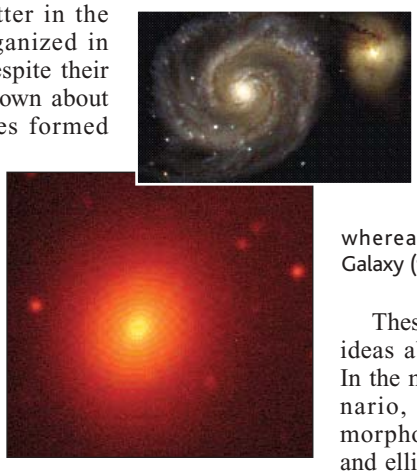
PERSPECTIVES: ASTRONOMY

Toward Resolving the Mystery of Galaxy Formation

Marco Scodeggio

Most visible matter in the universe is organized in galaxies. Yet despite their prominence, little is known about how and when galaxies formed and how they evolved. New evidence is now shedding light on galaxy formation processes in the distant universe, indicating that an answer may be within reach.



Common types of galaxies. These nearby galaxies are easily classified by eye according to their morphological appearance. The elliptical galaxy M32 (**bottom**) is distinctly red, whereas the spiral Whirlpool Galaxy (**top**) is much bluer.

There are two basic models for galaxy formation. In the monolithic collapse scenario, all galaxies were formed in a single event, through the gravitational collapse of a cloud of primordial gas, very early in the history of the universe (*1*, *2*). In the hierarchical merging scenario, galaxies are gradually assembled through multiple mergers of smaller subgalactic units, a process that continues from the early universe to the current epoch (*3*, *4*).

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These differences extend to ideas about galaxy evolution. In the monolithic collapse scenario, galaxies of different morphological types (spirals and ellipticals) are born intrinsically different, whereas in the hierarchical merging scenario, galaxies end up as spirals or ellipticals depending on the details of their merger history. As a result, the first model predicts that the number of galaxies of a given type should be approximately constant at all redshifts (that is, throughout the history of the universe), whereas the second predicts that there number should decrease with increasing redshift (that is, decreasing age).

Attempts to discriminate between the two models focus mostly on elliptical