MATERIALS SCIENCE

Flexible Electronics

Inkjet printing of metal wires yields bendable electrical connections for use in flexible electronic devices.

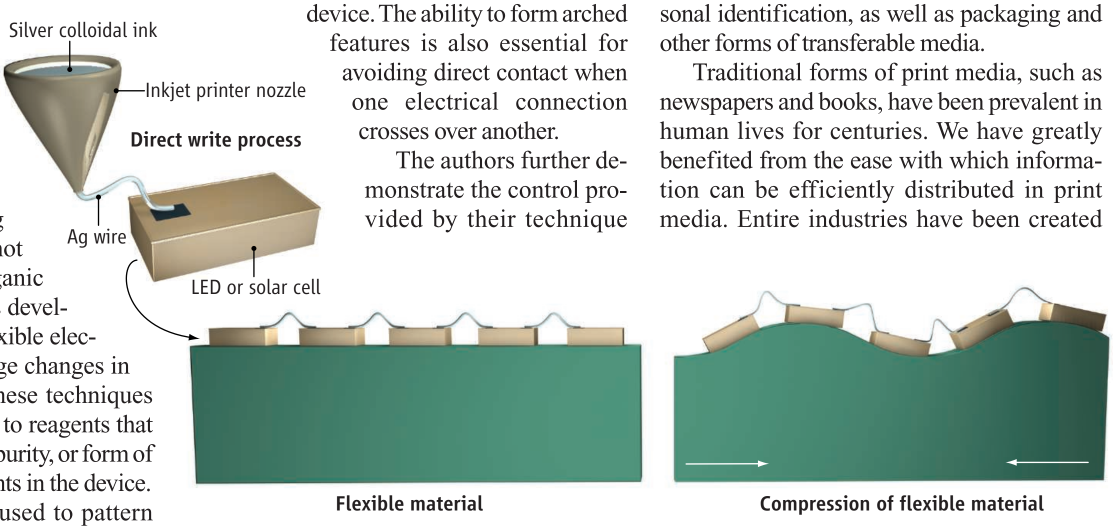
Byron D. Gates

Organic polymers are the main components of most flexible electronic devices. These devices rely on the compliant physical properties of organic polymers to maintain electrical continuity when deformed. Electrical connections within these devices are a point of weakness and have limited the types of materials and processes that can be used. Although inorganic semiconductors and metals have high conductivity, these materials will not commonly sustain repeated bending or stretching. On page 1590 of this issue, Ahn *et al.* (*1*) show how metal can be added to components within flexible electronic devices, enabling conductivity to be maintained even after repeated deformation.

Connections between electronic structures have traditionally been designed with a planar architecture that is patterned through multiple fabrication steps (*2*, *3*). Much of the fabrication technology used in flexible electronics was initially borrowed from existing device fabrication platforms, such as those used to manufacture silicon-based thin-film transistors. These techniques largely depend on the selective liftoff or etching of materials, using process conditions that are not always compatible with organic polymers. Process techniques developed for the fabrication of flexible electronic devices must avoid large changes in temperature and pressure. These techniques must also minimize exposure to reagents that may degrade the conductivity, purity, or form of the organic polymer components in the device.

Inkjet printing has been used to pattern organic semiconductors (*4*), metal contacts on organic semiconductors (*5*–*7*), and metallic structures (*8*) that require minimal further processing. Ahn *et al.* have now used inkjet printing to create three-dimensional (3D) metallic connections between functional components of flexible devices (see the figure). The authors first fine-tuned a colloidal ink of silver nanoparticles by adjusting the uniformity of the particles, the viscosity of the ink, and the drying time of the solvents. They then extruded the ink through a nozzle that directed the selective deposition of silver particles onto the flexible substrate. After annealing at 250°C for ≤30 min, the printed wires exhibited an electrical resistivity nearing that of bulk silver. Annealing can also be done using light or microwaves (*9*, *10*). The resistivity of the printed silver wires is about two orders of magnitude lower than that of commonly used conductive organic polymers (*1*). This improvement translates into lower power consumption and a lower heat load on the surrounding environment for devices incorporating these printed wires.

Controlling the deposition of the colloidal silver ink is essential for fabricating free-standing wires that have both 2D and 3D components. The electrical connections demonstrated by Ahn *et al.* include springs and structures with built-in slack to accommodate the stretching and bending of a flexible device. The ability to form arched features is also essential for avoiding direct contact when one electrical connection crosses over another.



Flexible material

Compression of flexible material

Flexible electrical metal connections. Wires connecting components within a flexible device can be fabricated by a direct-write process using inkjet printing of silver nanoparticles. As shown by Ahn *et al.*, the technique can be used to fabricate three-dimensional connections that span between components of a flexible device and that flex when the device is deformed.

The authors further demonstrate the control provided by their technique by reporting silver wires with width-to-length ratios up to 1:1000. These wires can span gaps up to 1 cm wide. The narrow dimensions of the printed wires (from ~2 to ~10 µm) are an additional benefit of this fabrication process. These small dimensions minimize the footprint of the electrical contact lines, which decreases the impact of the wires on the optical quality of the device and increases the density of features in the device. Although inkjet printing is a serial process, Ahn *et al.* have demonstrated a wide range of benefits for this technology.

Flexible electronic devices compete with paper-based media as well as existing electronic media. It is desirable to find a technology platform that can be rolled or bent (as with paper), yet robust enough to be unfurled and reused. The end use of the device will depend on the functions incorporated into its architecture. Ahn *et al.* demonstrate a few features that might be desirable in a flexible device, including optical and optoelectronic components such as light-emitting diodes (LEDs) and solar cells. Tuning the optical properties of a flexible device is widely recognized as necessary, with research efforts directed toward both emissive and reflective properties (*2*, *3*, *11*). Other applications of flexible device technology include radio frequency identification (RFID) tags and antennas that can be incorporated into personal identification, as well as packaging and other forms of transferable media.

Traditional forms of print media, such as newspapers and books, have been prevalent in human lives for centuries. We have greatly benefited from the ease with which information can be efficiently distributed in print media. Entire industries have been created around the printing, distribution, and storage of paper articles. Overcoming our dependence on paper will require its replacement with a technology that is comparable to paper in its weight, flexibility, and ease of use. Key technologies are necessary to enable the manufacture of such an alternative form of media. The work of Ahn *et al.* is a transition from typical models of fabrication, providing possibilities

---

Department of Chemistry, Simon Fraser University, Burnaby, British Columbia V5A 1S6, Canada. E-mail: bgates@sfu.ca

for incorporating multiple functions into a single flexible device.

Flexible electronic devices are becoming commonplace in our lives. Screens that can flex or otherwise distort have been incorporated into laptops, televisions, and mobile phones. Lightweight electronic display devices that can be rolled up for storage are being developed. The achievement of completely converting to a paperless society will be revolutionary in itself, but so are the technological advances necessary to make this new form of media commonplace in our daily lives.

References

1. B. Y. Ahn *et al.*, *Science* **323**, 1590 (2009); published online 12 February 2009 (10.1126/science.1168375).
2. S. R. Forrest, *Nature* **428**, 911 (2004).
3. E. Menard *et al.*, *Chem. Rev.* **107**, 1117 (2007).
4. H. Sirringhaus *et al.*, *Science* **290**, 2123 (2000).
5. Y. Noguchi, T. Sekitani, T. Yokota, T. Someya, *Appl. Phys. Lett.* **93**, 043303 (2008).
6. D. Kim, S. Jeong, H. Shin, Y. Xia, J. Moon, *Adv. Mater.* **20**, 3084 (2008).
7. S. Gamerith *et al.*, *Adv. Funct. Mater.* **17**, 3111 (2007).
8. J. E. Smay, J. Cesarano III, J. A. Lewis, *Langmuir* **18**, 5429 (2002).
9. J. Yun *et al.*, *Jpn. J. Appl. Phys.* **47**, 5070 (2008).
10. J. Perelaer, B.-J. de Gans, U. S. Schubert, *Adv. Mater.* **18**, 2101 (2006).
11. B. Comiskey, J. D. Albert, H. Yoshizawa, J. Jacobson, *Nature* **394**, 253 (1998).

10.1126/science.1171230

IMMUNOLOGY

Two-in-One Designer Antibodies

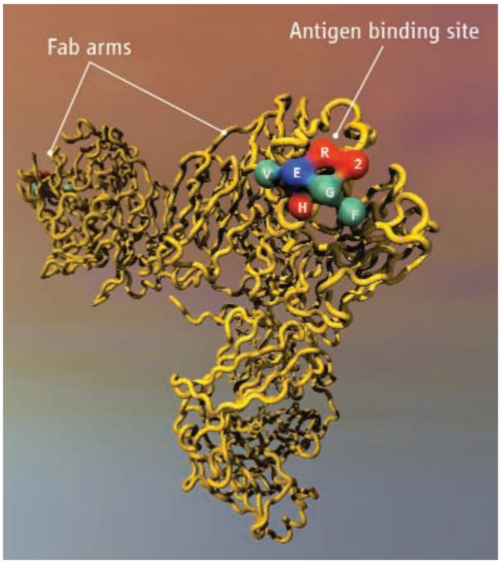
Paul W. H. I. Parren[1] **and Dennis R. Burton**[2]

An antibody is engineered to recognize two different proteins with high affinity, opening the door to improved combination therapies for cancers and infections.

Cancer and certain infectious diseases such as HIV-1/AIDS that are characterized by genetic heterogeneity are often difficult to treat with a single therapeutic agent. Combination therapies that target multiple disease-associated molecules are therefore widely deployed. For example, mixtures of antibodies are being tested for clinical use, despite high development, manufacturing, and treatment costs. The requirement for multiple antibodies is based on the prevailing one antibody-one antigen dogma. On page 1610 in this issue, Bostrom *et al.* (*1*) overthrow this dogma and describe a new "two-in-one" designer antibody concept in which the same binding site on an antibody is engineered to recognize two different antigens, both with high affinity.

The two antigens studied by Bostrom *et al.* are vascular endothelial growth factor (VEGF) and human epidermal growth factor receptor 2 (HER2), representing well-known tumor targets. VEGF promotes blood-vessel formation for the growing tumor and is targeted by the antibody bevacizumab (Avastin), commonly used to treat colorectal cancer. HER2 is highly expressed by some breast tumors and is targeted by the antibody trastuzumab (Herceptin). The authors show that an engineered antibody binds tightly to both antigens and inhibits the growth of both VEGF- and HER2-dependent tumors in animal models. The potential applications of the approach will need very careful exploration but will surely have far-reaching impact.

Bostrom *et al.* generated the two-in-one antibody by expressing the HER2-specific antibody trastuzumab on the surface of filamentous bacteriophage. Random nucleotide sequence was incorporated into the gene segments encoding the antigen-binding loops of the light chain to generate a large phage library. The library was selected for binding to HER2 and VEGF to generate a panel of two-in-one antibodies of varying affinity.



Two for the price of one. An antibody consists of four polypeptides, two heavy and two light chains, that form two "Fab arms." Each arm harbors an antigen binding site, formed by loops from the heavy and light chains. The binding site in the two-in-one antibody shown can interact with HER2 (red) and VEGF (green) through mostly unique, but also some shared (blue), elements. When affinity-matured, the antibody inhibits both HER2 and VEGF activity in vitro and in vivo. The source of the structure shown is antibody IgG1 b12 (*16*), RCSB PDB accession code 1HZH. The molecule was rendered using VMD software and further modeled with 3D software (Bryce 6.1). Refining and colors were done with Adobe Photoshop CS3.

CREDIT: JOOST BAKKER/GENMAB BV

High-resolution crystal structures of one of these antibodies in complex with either VEGF (dissociation constant $K_d = 300$ nM) or HER2 ($K_d = 26$ nM) were solved to elucidate the mechanism of "two-in-one" binding at the molecular level. The binding surface on the antibody for each antigen overlapped, but within the buried surface of each binding site, distinct amino acids contributed to the binding strength for each antigen: VEGF binding was primarily mediated by light-chain residues and HER2 binding by heavy-chain residues. The overlapping binding areas indicate that each antibody binding site cannot bind both antigens simultaneously (see the figure). The antibody binding sites in the two-in-one antibody are therefore selectively promiscuous; each can interact with two different partners, but will only bind to one at a time. For subsequent studies, an affinity improved two-in-one antibody (VEGF $K_d = 3$nM, HER2 $K_d = 0.2$ nM) was generated.

Approaches to generate antibody molecules with multiple binding moieties have been tried before, with varying success. Such molecules were engineered by "fusing" two or more antibody binding sites into a single molecule to increase binding avidity or bind multiple antigens (*2*, *3*). Antibodies binding two antigens can also be generated by Fab arm exchange, which occurs naturally in vivo for immunoglobulin G4 molecules (*4*), or can be created in vitro by cell fusion or antibody engineering (*5*). Antibodies in which two binding sites recognizing distinct antigens are connected to a single Fab arm represent another permutation (*6*). An example that is perhaps the closest comparable break with the one antibody–one antigen dogma comes from chemically

---

[1] Genmab, Yalelaan 60, 3584 CM Utrecht, Netherlands. [2] Department of Immunology and Microbial Science and IAVI Neutralizing Antibody Center, The Scripps Research Institute, La Jolla, CA 92037, USA. E-mail: p.parren@genmab.com, burton@scripps.edu

Published by AAAS