product. The ability of RNA to provide general acid-base catalysis was discovered only last year (*9,10*) in studies involving the hepatitis delta virus ribozyme (*11*).

Efficient general acid-base catalysis requires that the acid-base have a pK_a around pH 7.0, whereas the adenine base titrates at or below pH 3.5. However, it is already known that certain RNA structures can perturb the pK_a of adenine toward a neutral pH (*12*). In addition, as Muth *et al.* (*13*) report on page 947 of this issue, experimental analysis of the nucleotides within the peptidyl transferase center demonstrates that the adenine implicated by the crystal structure has an unusual pK_a of 7.6. Remarkably, two RNAs—identified by in vitro evolution for their ability to catalyze peptidyl transfer (*14*) or to bind the analog of the reaction intermediate (*15*)—have adenines in a local sequence and secondary structure similar to that of the critical adenine in the ribosome. So, this pair of RNAs may recapitulate the key feature of the rRNA reaction mechanism.

Of course, general acid-base catalysis can easily be provided in the active site of a protein enzyme, which leads to the question: Why does nature use RNA catalysis to achieve protein synthesis? One argument is evolutionary. If, indeed, there was an early RNA world where RNA provided both genetic information and catalytic function, then the earliest protein synthesis would have had to be catalyzed by RNA. Later, the RNA-only ribosome/ribozyme may have been embellished with additional proteins; yet, its heart of RNA functioned sufficiently well that it was never replaced by a protein catalyst. But there are persuasive chemical arguments as well. The substrates of the ribosome are RNAs—aminoacylated tRNAs and an mRNA—and RNA is particularly well suited for specific recognition of other RNAs through formation of base pairs, base triples, and other interactions. Furthermore, RNA is well suited to perform very large-scale conformational changes, and such movements are required for protein synthesis.

These most recent contributions of Steitz, Moore, and colleagues provide a milestone, but not the finish line. This one structure contains more RNA-RNA and RNA-protein interactions than all previous atomic-level structures combined, so ribophiles can look forward to years of additional analysis. The whole ribosome needs to be brought to this same atomic level of resolution, and the proposed reaction mechanism deserves critical testing. Finally, the molecular basis of the mRNA translocation step that must occur after each peptidyl transfer event remains obscure. Thus, although the current crystal structure provides one beautiful frame, we still look forward to seeing the entire movie.

References

1. N. Ban, P. Nissen, J. Hansen, P. B. Moore, T. A. Steitz, *Science* **289**, 905 (2000).
2. P. Nissen, J. Hansen, N. Ban, P. B. Moore, T. A. Steitz, *Science* **289**, 920 (2000).
3. N. Ban *et al.*, *Nature* **400**, 841 (1999).
4. W. M. Clemons Jr., *et al.*, *Nature* **400**, 833 (1999).
5. J. H. Cate, M. M. Yusupov, G. Z. Yusupova, T. N. Earnest, H. F. Noller, *Science* **285**, 2095 (1999).
6. H. F. Noller *et al.*, *Nucleic Acids Res.* **9**, 6167 (1981).
7. M. Welch, J. Chastang, M. Yarus, *Biochemistry* **34**, 385 (1995).
8. H. F. Noller, V. Hoffarth, L. Zimniak, *Science* **256**, 1416 (1992).
9. A. T. Perrotta, I.-H. Shih, M. D. Been, *Science* **286**, 123 (1999).
10. S. Nakano, D. M. Chadalavada, P. C. Bevilacqua, *Science* **287**, 1493 (2000).
11. A. R. Ferre-D'Amare, K. Zhou, J. A. Doudna, *Nature* **395**, 567 (1998).
12. P. Legault and A. Pardi, *J. Am. Chem. Soc.* **119**, 6621 (1997).
13. G. W. Muth, L. Ortoleva-Donnelly, S. A. Strobel, *Science* **289**, 947 (2000).
14. B. Zhang and T. R. Cech, *Chem. Biol.* **5**, 539 (1998).
15. M. Welch, I. Majerfeld, M. Yarus, *Biochemistry* **36**, 6614 (1997).

PERSPECTIVES: MATERIALS PROCESSING

The Power of Direct Writing

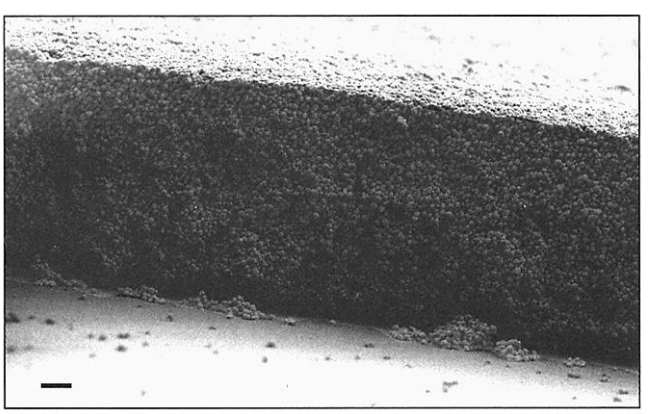
Douglas B. Chrisey

Direct-write technologies are of increasing importance in materials processing, enabling, for example, the simplification of printed circuit board manufacture at reduced costs (*1*). In a direct-write approach, structures are built directly without the use of masks, allowing rapid prototyping. As materials and processing challenges are being met with increasing success, direct-write techniques move toward a wide range of applications. Passive electronic components and interconnects have been made by direct-write techniques using a variety of materials. In a parallel development, direct writing of biomaterials is used for tissue engineering and array-based biosensors.

To optimize different direct-write techniques, electronic materials and approaches must be tailored for each processing method, transfer method, and required electronic or other device performance. Many different approaches exist to direct-write or transfer patterned materials, and each technique has its own merits and shortcomings. The techniques include plasma spray, laser particle guidance, matrix-assisted pulsed-laser evaporation (MAPLE), laser chemical vapor deposition (CVD), micropen, ink jet, e-beam, focused ion beam, and several novel liquid or droplet microdispensing approaches (*2–9*).

One theme common to all techniques is their dependence on high-quality starting materials, typically with specially tailored chemistries and/or rheological properties (such as viscosity, density, and surface tension). The starting materials, sometimes termed "pastes" or "inks," may consist of combinations of powders, nanopowders, flakes, surface coatings, organic precursors, binders, vehicles, solvents, dispersants, and surfactants. These materials have applications as conductors, resistors, and dielectrics and are being developed specifically for low-temperature deposition (<300° to 400°C). They will allow fabrication of passive electronic components and radio frequency devices with the performance of conventional thick film materials, but on low-temperature flexible substrates, such as plastics, paper, and fabrics. The desired final electronic materials may be silver, gold, palladium, and copper conductors or alloys; polymer thick film and ruthenium oxide–based resistors; and metal titanate-based dielectrics.

Problems arise, however, because the fabrication of high-quality crystalline materials—required for high electronic performance of the final material—is nearly impossible at



Tight packing. This scanning electron micrograph of a fracture cross section demonstrates the extremely uniform and optimized packing of $BaTiO_3$ nanopowders. The individual powder particles have assembled to produce a dense dielectric layer.

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these processing temperatures (~400°C). The highest possible packing density for spherical powders is ~74% for the face-centered cubic structure and is even lower (~64%) for random close packing (*10*, *11*). This means that there is at least 26% air in the structure. According to the logarithmic mixing rule for dielectrics, 26% air reduces the effective dielectric constant by almost an order of magnitude, highlighting the importance of reducing the porosity in transferred materials (*12*).

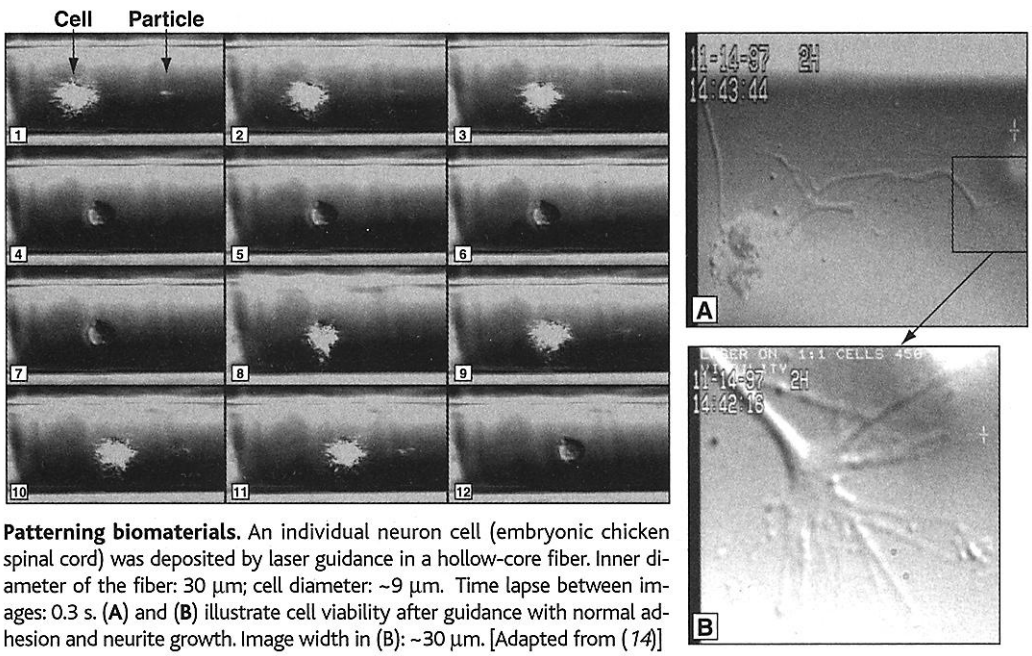
One strategy to overcome this liability, which most of the aforementioned techniques can use to some extent, is to begin with a high-density packed powder of differing particle sizes (see the first figure) combined with chemical precursors that form low–melting point nanoparticles in situ, welding the powder together chemically (*13*). The precursor chemistries used are diverse and include various thermal, photochemical and vapor, liquid, and/or gas coreactants. The precursor chemistries carefully avoid incorporation of carbon and hydroxide (which would cause high losses at microwave frequencies) and chemistries that are incompatible with other fabrication line processing steps.

To further improve the electronic properties for low-temperature processing, especially of oxide ceramics, laser surface sintering is used to enhance particle-particle bonding and reduce porosity. For infrared laser wavelengths (1 to 10 μm), the penetration depth is very dependent on laser and material properties, but for most combinations is between 1 and 10 micrometers. Annealing just the surface brings with it the benefits of higher temperature processing on thermally sensitive, but technologically important, substrates.

In most cases, individual direct-write techniques make trade-offs between increasing particle bonding to help the transfer process and optimizing direct-write properties such as resolution or speed. The resolution of direct-write lines can be on the micrometer scale, speeds can be greater than 200 mm/s, and the electronic material properties are comparable to those of conventional screen-printed materials. The use of electronic materials that have been optimized for direct-write technologies results in deposition of finer features, minimal process variation, lower prototyping and production costs, higher manufacturing yields, decreased prototyping and production time, greater manufacturing flexibility, and reduced capital investments.

Materials advances have driven the direct writing of electronic materials. In contrast, recent advances in the direct writing of biomaterials have been driven by advances in the transfer technology, in particular, the recognition that in some cases the transfer process can be extremely gentle. Laser-guided particle deposition has the ability to deposit almost any material on any substrate with micrometer-scale accuracy. This technique has been applied to the deposition of individual "living" neural cells (see the second figure). The deposited cells remained viable in spite of being exposed to the laser transfer process (*14*, *15*). Micrometer-scale patterns of viable cells and the methods to manufacture them are required for next-generation tissue engineering, fabrication of cell-based microfluidic biosensor arrays, and selective separation and culturing of microorganisms. There is currently no technology capable of writing adjacent patterns of different viable cells. At the Naval Research Laboratory, patterns of viable *Escherichia coli* bacteria have been transferred onto various substrates with a laser-based forward transfer technique (*16*). We are now in a position to use these tools to create three-dimensional mesoscopically engineered structures of living cells, proteins, DNA strands, and antibodies and to cofabricate electronic devices on the same substrate to rapidly generate cell-based biosensors and bioelectronic interfaces. This will, for example, allow us to probe intercellular signaling. These methods represent an important advance in biomaterial processing and the manipulation of natural systems.

Current progress in many direct-write technologies is driven by advances in the transfer and processing of novel materials. These technologies offer opportunities in manufacturing improved discrete electronic devices and rapid prototyping machines with increased flexibility, the fabrication of flexible electronics, and the culturing of abnormal or cancerous cells (*17*, *18*). Future work in this area will focus on lowering the processing temperature and increasing the density and particle-particle bonding to improve the electronic properties.



Patterning biomaterials. An individual neuron cell (embryonic chicken spinal cord) was deposited by laser guidance in a hollow-core fiber. Inner diameter of the fiber: 30 μm; cell diameter: ~9 μm. Time lapse between images: 0.3 s. (**A**) and (**B**) illustrate cell viability after guidance with normal adhesion and neurite growth. Image width in (B): ~30 μm. [Adapted from (*14*)]

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References

1. A. R. Ehsani and M. Kesler, *IEEE Spectrum* (May 2000), p. 40.
2. H. Esrom, J.-Y. Zhang, U. Kogelschatz, A. J. Pedraza, *Appl. Surf. Sci.* **86**, 202 (1995).
3. M. J. Renn, R. Pastel, H. J. Lewandowski, *Phys. Rev. Lett.* **82**, 1574 (1999).
4. P. Blazdell and S. Kurdoda, *Surf. Coat. Tech.* **123**, 239 (2000).
5. M. K. Herndon, R. T. Collins, R. E. Hollingsworth, P. R. Larson, M. B. Johnson, *Appl. Phys. Lett.* **74**, 141 (1999).
6. H. Herman and S. Sampath, *Industr. Ceram.* **18**, 29 (1999).
7. B. H. King, D. Dimos, P. Yang, S. L. Morissette, *J. Electroceram.* **3**, 173 (1999).
8. D. B. Chrisey *et al.*, *Appl. Surf. Sci.* **154**, 593 (2000).
9. J. M. Fitz-Gerald *et al.*, *Appl. Phys. Lett.* **76**, 1386 (2000).
10. S. Torquato, T. M. Truskett, P. G. Debenedetti, *Phys. Rev. Lett.* **84**, 2064 (2000).
11. O. Pouliquen, M. Nicolas, P. D. Weidman, *Phys. Rev. Lett.* **79**, 3640 (1997).
12. M. P. McNeal, S.-J. Jang, R. E. Newnham, *Proc. IEEE Intl. Symp. Appl. Ferro.* **2**, 837 (1996).
13. P. Atanassova, K. Kunze, T. Kodas, M. Hampden Smith, Superior Micropowders, unpublished results.
14. D. Odde and M. J. Renn, *Biotechnol. Bioeng.* **67**, 312 (2000).
15. D. Odde and M. J. Renn, *Trends Biotechnol.* **17**, 385 (1999).
16. B. R. Ringeisen, D. B. Chrisey, A. Piqué, H. D. Young, R. Modi, M. Bucaro, J. Jones-Meehan, B. J. Spargo, unpublished results.
17. X. Yan and P. Gu, *Computer-Aided Design*, **28**, 307 (1996).
18. R. Maddox and J. Knesek, *Aerospace Am.* **31**, 28 (1993).