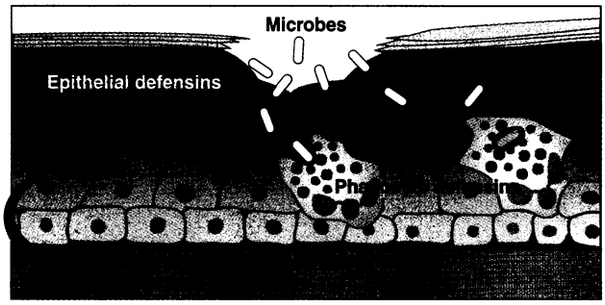
pancreas and other epithelial sites; HBD-2 is induced in skin and other epithelia during inflammation (see figure on this page). At submicromolar concentrations, these defensins attracted both immature dendritic cells and memory T cells, which initiate a primary and recall immune response, respectively. The effect was evidently mediated by the CCR6 chemokine receptor because β-defensins effectively competed with the receptor's ligand, MIP-3α. If the same mechanism functions in vivo, the release of these two defensins from injured epithelial cells would recruit dendritic cells and memory T cells to infected tissues, thereby promoting the development of adaptive (antibody and T cell–mediated) immunity. Like the β-defensins, human neutrophil α-defensins also attract T cells. In addition, some defensins also block the adrenocorticotrophin receptor and could inhibit the production of the immunosuppressive adrenal steroid hormones during acute infection (*13*). The ability of some defensins to act as signaling molecules could explain their biological effects when their concentrations are too low to be directly microbicidal.



Inflamed defenders. A model of defensin activity in an infected epithelium. Epithelial cells synthesize antimicrobial defensins (red) both constitutively and in response to infectious and inflammatory stimuli. Other defensins are introduced by the influx of phagocytic cells that use them to kill ingested microbes. Released defensins attract dendritic cells and memory T cells, setting the stage for the adaptive phase of the immune response.

Comparison of defensin genes across vertebrate species indicates that they are rapidly evolving. As variations in defensin sequences and patterns of tissue expression bring out distinct aspects of defensin biology in each species, studies of defensins in diverse animals have often provided crucial insights. The article by Tang *et al.* on page 498 (*5*) reports on studies of white cell defensins in the rhesus monkey. Several of the defensins isolated from rhesus white cells resembled their human counterparts, but one was unique and initially refractory to conventional analysis. The puzzle was solved brilliantly when the investigators determined that they were dealing with a cyclic peptide generated by head-to-tail peptide splicing of the products of two similarly truncated α-defensin genes! Although otherwise similar to α-defensins with their six cysteines, these novel defensin genes contained a "premature" stop codon in the segment after the third cysteine. This resulted in generation of two abbreviated defensin molecules that each donated 9 amino acids to the final, 18–amino acid cyclic product: a θ-defensin stabilized by three parallel disulfide bonds. This remarkable feat of posttranslational processing could be reconstituted by transfecting HL-60 human leukemia cells with the two defensin cDNAs. This elegant model should provide the requisite tools that will allow the processing and splicing mechanism to be worked out. The new θ-defensin molecule resembles porcine white cell protegrins, hairpin-shaped peptides with 16- to 18-amino acid residues and two disulfide bonds (*14, 15*). Like protegrins, θ-defensins retain full activity at salt concentrations present in blood, a feature that makes them interesting candidates for development as antibiotics.

Despite advances in prevention, diagnosis, and treatment, infectious diseases continue to challenge us. We are facing the limitations of vaccine-based immunization strategies and the increasing resistance of microbes to existing antibiotics. The renaissance of research into innate host defense mechanisms that do not depend on specific recognition of individual antigens offers the promise that some of the many substances that mediate the innate resistance of plants and animals to infections may prove useful as templates for new antibiotics or immunostimulants.

References

1. J. Marsh and J. A. Goode, Eds., *Antimicrobial Peptides*, Ciba Foundation Symposium 186 (Wiley, Chichester, UK, 1994).
2. J. A. Hoffmann, F. C. Kafatos, C. A. Janeway Jr., R. A. B. Ezekowitz, *Science* **284**, 1313 (1999).
3. T. Ganz and R. I. Lehrer, *Curr. Opin. Immunol.* **10**, 41 (1998).
4. D. Yang *et al.*, *Science* **286**, 525 (1999).
5. Y.-Q. Tang *et al.*, *ibid.*, p. 498.
6. C. L. Wilson *et al.*, *ibid.*, p. 113.
7. T. Ganz and R. I. Lehrer, *Pharmacol. Ther.* **66**, 191 (1995).
8. A. J. Ouellette and M. E. Selsted, *FASEB J.* **10**, 1280 (1996).
9. E. V. Valore, E. Martin, S. S. Harwig, T. Ganz, *J. Clin. Invest.* **97**, 1624 (1996).
10. K. W. Bensch, M. Raida, H. J. Magert, P. Schulz-Knappe, W. G. Forssmann, *FEBS Lett.* **368**, 331 (1995).
11. J. Harder, J. Bartels, E. Christophers, J.-M. Schroeder, *Nature* **387**, 861 (1997).
12. E. V. Valore *et al.*, *J. Clin. Invest.* **101**, 1633 (1998).
13. S. Solomon *et al.*, *J. Steroid Biochem. Mol. Biol.* **40**, 391 (1991).
14. V. N. Kokryakov *et al.*, *FEBS Lett.* **327**, 231 (1993).
15. R. I. Fahrner *et al.*, *Chem. Biol.* **3**, 543 (1996).

PERSPECTIVES: DEVICE PHYSICS

In Search of Low-*k* Dielectrics

Robert D. Miller

Within the next few years, high-performance chips containing as many as 0.5 billion transistors on a single chip will be produced. These advanced chips may contain up to 10,000 m of on-chip wiring connecting the individual devices with each other and with the outside world. However, such increased device and wiring densities cannot be achieved with currently used materials. The search is now on for materials that can replace silicon dioxide as the insulator in these future devices. But despite a bewildering number of candidate materials under investigation, a clear winner has yet to emerge.

In a typical microchip, layers of copper interconnect wiring are separated by a dielectric insulator, traditionally silicon dioxide (see the figure). Both the resistance of the metal and the capacitance of the insulator increase markedly as the wiring dimensions and pitch decrease, resulting in crosstalk and capacitative coupling between the metal interconnect lines and thus increased signal delays (*1*). Several semiconductor manufacturers have demonstrated recently that the traditional Al(Cu) wiring can be replaced by pure copper, which has a resistivity only 60% of that of aluminum (*2*). Performance gain is then limited by the intra- and interlayer capacitance, dictated primarily by the dielectric constant of the insulator. This has fueled the frantic search for new dielectric insulators with lower dielectric constants k than silicon dioxide ($k = 3.9$ to 4.2) (*3*).

Any replacement low-k material must meet the current integration requirements, such as thermal stability in excess of 400°C, good mechanical properties, low ion content, breakdown fields in excess of 2

The author is at IBM Research Division, Almaden Research Center, San Jose, CA 95120–6099, USA. E-mail: rdmiller@almaden.ibm.com

MV/cm, low water uptake, lithographic processability, low thermal expansion coefficients and film stresses, good adhesion to a variety of substrates, and low reactivity with conductor metals at elevated temperatures. Because of the difficulties associated with changing both the metal and the insulator materials simultaneously, advanced devices in the near term will first use copper and SiO_2. New low-k materials will be introduced subsequently, and the dielectric constant of the low-k insulators will be lowered progressively with succeeding device generations, ultimately approaching a value of 1.0 represented by a true air bridge. Given the extraordinary difficulties and costs associated with introducing a new dielectric insulator, the "Holy Grail" for manufacturing would be a material with dielectric generational extendibility: a group of insulators with similar material properties differing primarily in the effective dielectric constant.

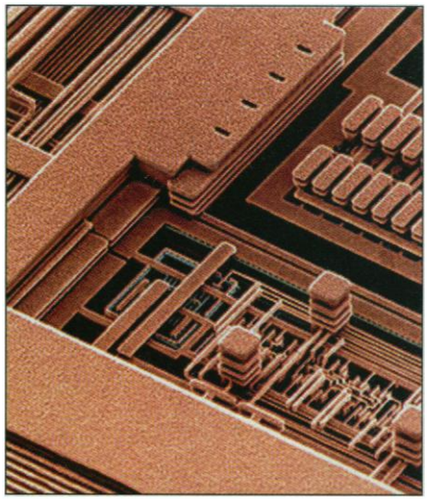
Several classes of insulating materials are currently under consideration as replacements for silicon dioxide. They can be roughly classified as inorganic-like or organic. Deposition methodology is also an important distinguishing factor. Until now, insulator deposition has been accomplished by plasma processes, chemical vapor deposition, or combinations of the two. Processes using these gas phase deposition techniques are generally well controlled, but the equipment is expensive. A potentially cheaper alternative is solution spin-on technology, which is used extensively for the application of thin-film photoresist materials.

In general, three material generations can be distinguished: materials with dielectric constants $k > 3.0$, $k = 2.5$ to 3.0, and $k < 2.2$. There are several promising candidates, for both vapor and spin-on deposition, at $3.0 < k < 4.0$ and in the low-k midrange (2.5 to 3.0) (see supplementary material), but relatively few dielectric candidates for the ultimately required ultra–low-k materials ($k < 2.2$). Also, none of the materials ensure generational extendibility and continuity of processing methodology, with the possible exception of porous materials.

Among the homogeneous polymers, only highly fluorinated alkane derivatives reach the dielectric target of $k < 2.2$. For example, polytetrafluoroethylene (Teflon) films with dielectric constants of 1.9 to 2.1 can be spun from surfactant-stabilized aqueous microemulsions (*4*). Unfortunately, they are very soft, their thermal stability above 400°C is questionable. There are also serious concerns about the effect of fluorinated dielectrics on the interconnect metals and metal liners at elevated temperatures.

Porous materials may have dielectric constants in the ultra–low-k region. Porosity raises specific integration concerns, but it is clear that no true dielectric generational extendibility to the ultra–low-k region can be achieved without embracing the concept of porosity. Porosity may be classified as either closed or open cell, the latter characterized by interconnected pores. Ideally, the porosity of on-chip insulators should be closed cell, present at a level no higher than necessary to meet the dielectric constant objectives, uniformly distributed and controlled to the nanoscopic level.

Porous silica (SiO_2) prepared by catalyzed sol-gel polymerization of orthosilicate esters has received considerable attention. Solvent is removed from the gelled films by supercritical extraction (aerogels) (*5*) or solvent exchange and careful drying (xerogels) (*6*). However, both techniques are process intensive and yield highly porous (50 to 98%), hydrophilic, open-celled silica. Moreover, the high dielectric constant ($k = 4.0$ to 4.2) of the densified silica matrix requires high porosities (50 to 80%) to achieve an ultra low–dielectric constant. Large void volumes also adversely affect other important film properties such as thermal conductivity and stability.



Complex wiring on a small scale. Top-down view of an IBM seventh generation microchip. The silicon dioxide insulating layers have been selectively removed to reveal the complexity of the wiring schemes.

One of the more interesting approaches to generating porosity in thin films involves the removal of a nanodispersed, thermally liable pore generator (porogen) from a high-temperature matrix. Nanodispersed hybrids can be produced by the sol-gel polymerization of orthosilicate esters, templated by monomeric (*7*, *8*) or polymeric surfactants (*9*). These films are subsequently converted into mesoporous silica by calcination, and a variety of regular open-cell porous structures with dielectric constants < 2.2 can be generated. This approach has also been applied to the generation of polyimide nanofoams ($k = 2.2$ to 2.3) (*10*), with suitable block copolymers mediating the self-assembly of a nanodispersed thermally labile phase. The development of other classes of porous polymers is a topic of considerable current interest.

In principle, dielectric constants < 2.2 could be achieved at low to medium porosity levels if the intrinsic dielectric constant of the matrix material were substantially lower than that of SiO_2. For example, porous films of methylsilsesquioxane (MSSQ), which has a dielectric constant of 2.8, have been produced (*10a*, *11*, *12*). Nanoscopic inorganic-organic hybrids were generated by vitrifying low–molecular weight MSSQ derivatives templated by highly branched macromolecular porogens with controlled molecular architectures. Dielectric constants in the 2.0 to 2.2 range were achieved at porosity levels of <20%, and the voids seem not to be interconnected.

The drive toward increased device densities and improved performance in the semiconductor devices makes the switch from SiO_2 on-chip insulators to low-k materials inevitable. Although there are a number of promising candidates for the advanced devices of the future, no clear winner emerges as yet among materials with dielectric constants < 3.0. Given the daunting integration challenges and costs associated with the introduction of a new dielectric, it is disturbing that there is no clearly defined route to dielectric generational extendibility. The introduction of porosity into dielectric materials provides, in concept, a route to dielectric generational extendibility into the ultra–low-k range. The switch to low-k, on-chip insulators continues to be a formidable challenge to chemists, physicists, materials scientists, and integration engineers.

References and Notes

1. S. R. Wilson *et al.*, in *Handbook of Multilevel Metallization for Integrated Circuits*, S. R. Wilson, C. J. Tracy, J. L. Freeman, Eds. (Noyes, Park Ridge, NJ, 1993), chap. 1.
2. D. Edelstein *et al.*, *Tech. Dig.* (1997), p. 376.
3. Chap. 4, in (*1*); P. Balk, *J. Non-Cryst. Solids* **187**, 1 (1995); J. Baliga, *Semiconductor International* (June 1998), p. 139.
4. C. T. Rosenmeyer and H. Wu, *Proc. Mater. Res. Soc.* **427**, 463 (1996); C. T. Rosenmeyer, J. W. Bartz, J. Hammes, *ibid.* **476**, 231 (1997).
5. L.W. Hrubesh *et al.*, *J. Mater. Res.* **8(7)**, 1736 (1993).
6. R. S. List *et al.*, *1997 Symp. on VLSI Technology (Digest of Technical Papers)* (1997), p. 77; C. Jin *et al.*, *Proc. Mater. Res. Soc.* **511**, 213 (1998).
7. P. J. Bruinsma *et al.*, *Proc. Mater. Res. Soc.* **443**, 105 (1996).
8. C. J. Brinker, *Curr. Opin. Solid State Mater. Sci.* **1**, 798 (1996).
9. D. Zhao *et al.*, *Science* **279**, 548 (1998); D. Zhao *et al.*, *J. Am. Chem. Soc.* **120**, 6024 (1998).
10. J. L. Hedrick *et al.*, *Adv. Polym. Sci.* **141**, 1 (1999); H.-J. Cha *et al.*, *Appl. Phys. Lett.* **68**, 1930 (1996). 10a. J. L. Hedrick *et al.*, *Adv. Mater.* **10(13)**, 1 (1998).
11. J. F. Remenar *et al.*, *Proc. Mater. Res. Soc.* **511**, 69 (1998).
12. C. V. Nguyen *et al.*, *Chem. Mater.*, in press.

References and Notes

[9] **Triblock Copolymer Syntheses of Mesoporous Silica with Periodic 50 to 300 Angstrom Pores**

Dongyuan Zhao; Jianglin Feng; Qisheng Huo; Nicholas Melosh; Glenn H. Fredrickson; Bradley F. Chmelka; Galen D. Stucky

Science, New Series, Vol. 279, No. 5350. (Jan. 23, 1998), pp. 548-552.

Stable URL:

http://links.jstor.org/sici?sici=0036-8075%2819980123%293%3A279%3A5350%3C548%3ATCSOMS%3E2.0.CO%3B2-M