Phase-Change Memories on a Diet

Martin Salinga, *et al.*

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T cell activation by a cell-intrinsic mechanism (*11*). CTLA-4 may also transduce signals via CD80 and CD86 into antigen-presenting cells and induce their production of an immunosuppressive metabolite, repress the transcription of the genes encoding CD80 or CD86, or inhibit the production of inflammatory cytokines, although how T cells evoke these events in antigen-presenting cells via CTLA-4 remains obscure (*12*).

CTLA-4 is a key molecular target for enhancing or damping immune responses clinically. CTLA-4 blockade by specific monoclonal antibody evokes effective immune response to tumors, and blockade of CD80 or CD86 by a CTLA-4–immunoglobulin fusion protein suppresses autoimmune responses and establishes transplantation tolerance (*13*, *14*). Assuming that CTLA-4 has multiple immune inhibitory roles, including trans-endocytosis of its ligands, further study of the cell-extrinsic and cell-intrinsic functions of this molecule will enable better control of physiological and pathological immune responses.

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APPLIED PHYSICS

Phase-Change Memories on a Diet

Device design helps reduce the power requirements for switching phase-change memory.

Martin Salinga and Matthias Wuttig

In 1637 René Descartes was pondering the possibilities of human-made machines, being certain that their potential would be very limited. It was inconceivable to him that a machine could ever "arrange words so as to adequately reply to what is said in its presence" (*1*). The recent competition between IBM's supercomputer Watson and two of the most successful *Jeopardy* champions demonstrates how far human-made machines have progressed. Nevertheless, Watson's success comes at appreciable cost: Whereas humans perform their daily duty of "thinking" by consuming an average power of only 50 W, Watson consumes more than 2 MW. Imagine how helpful computers could be if processing and storing data could be accomplished by much less power-hungry computers. On page 568 of this issue, Xiong *et al.* (*2*) demonstrate a remarkable step forward whereby a new design for phase-change memory can lead to a drastic reduction in the power requirements for its operation.

In phase-change materials, a short voltage pulse is used to heat the crystalline phase above the melting temperature; rapidly quenching the liquid creates an amorphous state with higher resistivity. Applying a second pulse with lower voltage switches the phase-change material back to the crystalline state, hence enabling rewritable data storage (*3*) (see the figure, panel B). This storage principle is nonvolatile—the information is not lost when the power to the storage medium is turned off. Because phase-change memories can also be very fast, comparable to the speed of volatile dynamic random access memories, they might provide the storage attributes of a universal memory, replacing several current memory technologies at once.

With greater demands to reduce the power needed to store and retrieve data, emphasis increasingly shifts to reducing the necessary pulse power to store data. Several approaches can reach this goal in phase-change memories. A particularly promising one is the reduction in the active volume of phase-change mate-

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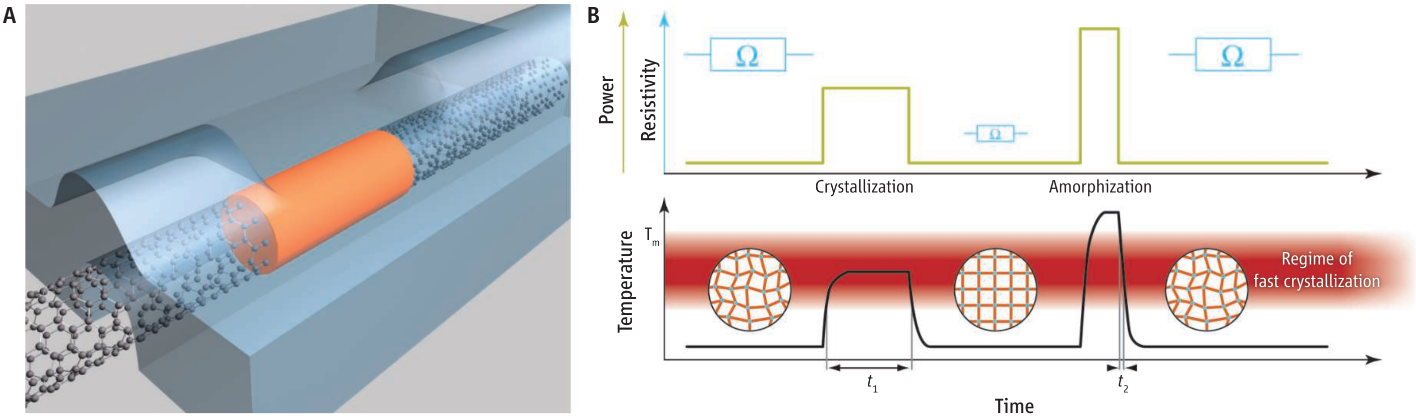

Memory switch. (**A**) A gap in a carbon nanotube lying on a substrate is filled by depositing a film of phase-change material (transparent blue) on top of the nanotube and its surrounding environment. The application of short current pulses switches only the well-defined volume in the gap of the nanotube. A large reduction in the active volume (orange cylinder) and especially of its contact area is achieved. (**B**) When the amorphous material is heated by an electrical current, its atoms become mobilized enough to find their way into the energetically more favorable crystalline state. The amorphization of a previously crystalline volume is obtained by heating above the melting temperature T_m and subsequent rapid cooling of the material, minimizing the time t_2 at temperatures that cause fast crystallization. The strong contrast in resistivity between the phases allows for an electrical determination of a cell's state.

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rial (*4*, *5*). Previous work has already shown that it is possible to scale phase-change memory cells down to the sub–20-nm technology node (*6*). The cross-sectional area of those cells, however, still exceeds 400 nm^2.

Xiong *et al*. investigate the power necessary to switch a region of phase-change material with a cross-sectional area of just 7 nm^2 with a clever trick of using extremely thin carbon nanotubes as electrodes. To build a phase-change memory cell, they briefly apply a high voltage to the ends of a carbon nanotube, which creates a gap in the nanotube, a few tens of nanometers wide. This gap is then filled by depositing a film of phase-change material on top of the nanotube and its surrounding environment. The subsequent application of short current pulses switches only the well-defined volume in the gap of the nanotube (orange cylinder in the figure, panel A).

With this approach, Xiong *et al*. investigate how the power necessary to store data in phase-change materials scales with the lateral extension of the region to be switched. The current necessary to amorphize (reset) a memory cell with a 7-nm^2 contact area is around 5 μA. This is at least one order of magnitude lower than the current required to switch more conventional memory cells with a contact area of around 400 nm^2. This remarkably low value demonstrates the excellent scaling potential of phase-change memories. But how much further can the contact area be reduced until a fundamental limit is approached? The work by Xiong *et al*. already pushes the cell size limit to 7 nm^2. Given the present speed of improvement in the semiconductor industry, it will take more than a decade until commercial cells will reach this size, extending the scaling potential of electronic data storage considerably.

Although the present approach focuses on the optimization of memory cells by reducing their volume, it should also be rewarding to improve phase-change materials further. Identifying materials with a relatively low melting temperature would be useful, as such materials need less power to be amorphized. Identifying materials with even lower thermal conductivity would ensure that little power is wasted to heat the surrounding region. Finally, materials that switch more rapidly would be desirable (*7*, *8*), as a reduction in the duration of applied electrical pulses will decrease the energy per switching event.

The results of Xiong *et al*. could help a future Watson to have less appetite for energy. Possibly this successor of Watson might even incorporate phase-change materials for a different reason. The ability to program variable resistance levels makes phase-change materials attractive for the development of neuromorphic hardware, a new class of hardware based on a computing logic more closely resembling the human brain. This strategy might bring humankind another step further toward a machine far beyond Descartes' imagination.

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BIOCHEMISTRY

The Two Faces of SAM

An unusual radical mechanism enables ribosome methylation in bacteria.

JoAnne Stubbe

The word "radical" (*1*) is often associated with highly energetic species (atoms or molecules) that chemically react with, and modify or destroy, molecules that they encounter. All organisms devote considerable metabolic effort to "control" radicals, such as reactive oxygen and nitrogen species (for example, the hydroxyl radical and nitric oxide), and to repair the damage that they inflict on macromolecules and small molecules alike. Radical-based reactions, however, also play an important role in metabolism. Evolution has produced mechanisms that harness radicals' reactivity to carry out difficult chemical transformations with exquisite specificity. For instance, while the common cellular compound called *S*-adenosylmethionine (SAM) is well known to play a role in the methylation of nucleophiles by a typical substitution reaction, in seminal work, Knappe and Schmitt (*2*) demonstrated that SAM mediates radical chemistry in organisms grown anaerobically (see the figure). Since then, investigators have implicated SAM in many unusual and diverse radical-based transformations.

On page 604 of this issue, Grove *et al*. (*3*) add to the list. They propose that SAM plays a central role in a novel radical chemical reaction that is involved in the development of antibiotic resistance in bacteria. They describe the unusual methylation of the C-2 and C-8 positions of an adenine (A2503) of the 23S rRNA (rRNA), catalyzed by two "methyltransferases," RlmN and Cfr. Both enzymes require two SAMs to transfer a single methyl group. These reactions appear to involve a typical nucleophilic methylation of a conserved cysteine (Cys_{355}-SCH_3 in RlmN) in each protein by SAM, followed by SAM-dependent radical chemistry that generates an unprecedented protein radical on the methylated cysteine (Cys_{355}-SCH_2•). In *Science* Express, Boal *et al*. (*4*) provide strong evidence for this proposal, presenting structures of RlmN involved in the reaction in the presence and absence of SAM.

The RlmN- and Cfr-catalyzed methylations described by Grove *et al*. add to the many novel reactions that involve radical chemistry and SAM (see the figure). In 2001, bioinformatic analyses by Sofia *et al*. (*5*) identified a new superfamily of enzymes, which they designated "radical SAM," whose members shared a CX_3CX_2C motif and SAM as a cofactor. There are now proposed to be >3000 members (*6*, *7*) of this family, including RlmN and Cfr. The family members share a requirement for a $[4Fe\text{-}4S]^{2+/1+}$ cluster with a unique Fe that binds SAM in a bidentate fashion through its α-amino and carboxylate groups (see the figure) (*8*). Each reaction involves the reductive cleavage of SAM to generate methionine (Met) and a 5′-deoxyadenosine radical (5′-dA•), the species responsible for initiation of the radical-dependent reactions. The 5′-dA• is used to remove a hydrogen atom (H•) (red spheres

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