The centriole induces the formation of centrosomes at specific times and in specific places, thus increasing the accuracy and speed of the processes the centrosome directs. For example, the centriole's orderly replication and splitting ensures that each cell inherits a single centrosome as it enters the cell cycle and duplicates this organelle before dividing. Cells lacking centrioles are more likely to make mistakes in chromosome segregation, thus threatening the survival of the cellular cooperatives they belong to. This danger can be prevented by evolving checkpoints that make completing cell division and starting the next round of DNA replication dependent on the presence of centrioles.

I suspect that this pattern is a common theme in the evolution of cellular processes. These processes first appear as slow and inaccurate self-assembly pathways that are governed by very simple rules. Subsequently, speed and fidelity evolve by adding components, such as centrioles, that direct or template what used to be self-assembly. To ensure that the improvements are used, cells evolve checkpoints that make initiating the process dependent on recruiting new components. If the requirements for efficiency are sufficiently high, the new and old components may be merged into the same structure, making both truly indispensable. This appears to have happened in the yeast spindle pole body, which has combined the functions of centrosome and centriole into a single indissoluble organelle. Another example of increasing template dependence is the centromere, the specialized region of the chromosome that attaches it to microtubules. At one extreme, the centromeres of *Drosophila* appear to assemble independently of the DNA sequence and are propagated by a process of self-assembly (*20*); those of mammals appear to be templated by specific DNA sequences under normal conditions but are capable of self-assembly as well. At the other extreme are budding yeast, which are absolutely dependent on specific DNA sequences to direct centromere assembly (*21*).

If the logic of progressive refinement and checkpoint dependence is correct, then many proteins and protein networks may be indispensable only because their absence activates checkpoints designed to guard against error. A checkpoint-independent requirement for other proteins may reflect the fuller integration of these newer components into previously self-sufficient trial-and-error processes. If repeated, such integrations could explain the evolutionary steps that converted the first forms of life into today's complex and sophisticated cells.

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PERSPECTIVES: ELECTRONICS

Toward Paperlike Displays

John A. Rogers

Low-cost electronic displays that look and feel like conventional printed paper will dramatically change the way we use and interact with laptop computers, personal digital assistants, and cellular telephones. They will also alter our notions of newspapers, magazines, greeting cards, and even cereal boxes, bumper stickers, and wallpaper.

Such "electronic paper" displays are radically different from traditional electronic systems, which rely on cathode ray vacuum tubes or liquid crystals with silicon-based circuitry on plates of glass. Electronic paper is a thin, high-contrast, reflective display that can be flexed, bent, rolled-up, and folded. A portable computer that uses this technology will resemble a pad of paper more closely than a standard laptop. Future printed paper products will retain the attractive appearance of conventional ink on paper but will be reconfigurable and reusable. A newspaper, for example, will consist of one or several sheets of electronic paper onto which information content, including animated images, will be downloaded through the wireless internet.

The technologies required for paperlike displays are just beginning to emerge from research laboratories in the form of realistic prototypes. The first sheets of electronic paper were recently demonstrated by Bell Labs and E Ink Corporation at the Fall 2000 meeting of the Materials Research Society (*1*). They incorporate the three new technologies that are essential for these types of systems: electronic "inks" for the optical component of the display, mechanically flexible transistors and circuits to drive the ink, and low-cost fabrication techniques to produce the circuits. The Bell Labs/E Ink displays use thin rubber-stamped plastic circuits and electrophoretic inks.

Two types of electronic inks are currently under development for commercial use in large-scale signs. One uses microencapsulated suspensions of charged white particles in a black fluid (*2*); the other relies on tiny rotatable balls that are white on one side and black on the other (*3*). Both are well-suited for electronic paper: They are thin (0.1 to 0.2 mm) and power efficient, they can support high-resolution images (more than 200 pixels per inch), and their contrast is better than newsprint.

To produce electronic paper displays, these "inks" must be laminated onto sheets of active matrix drive circuitry. These types of circuits use transistors at each pixel location to control the electric fields that determine the color of the "ink." They must be mechanically flexible and should be built on thin, low-cost plastic substrates. Meeting these requirements requires materials and patterning techniques that are completely different from those currently used in the microelectronics industry. Most plastics, for example, cannot survive the high-temperature deposition steps that are common for conventional silicon-based circuits. Also, plastic sheets typically have surfaces that are rougher and more uneven than traditional silicon or glass substrates. These and other characteristics make them difficult to process in traditional ways.

Over the last several years, substantial progress has been made toward materials and patterning methods for flexible electronics on plastic. Several classes of semiconductors can now be deposited on plastics at low temperatures: inorganics formed from solution or cast from colloidal suspensions, hybrid inorganic-organic materials, small molecule organics, and even polymers (*4*). A few of them

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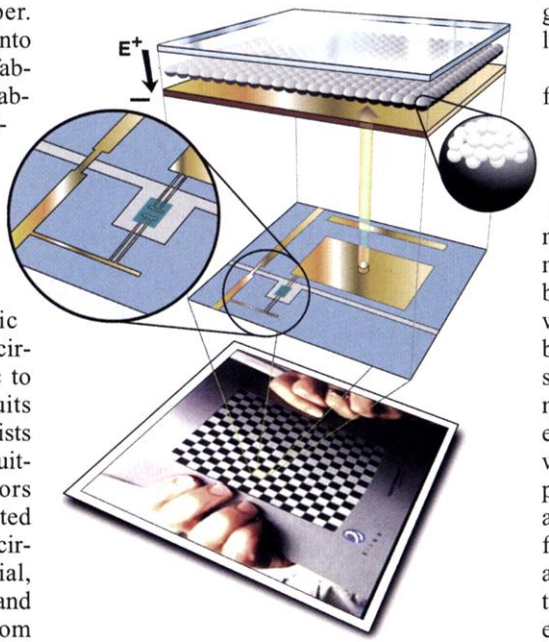
seem to be useful for electronic paper. They have recently been incorporated into small laboratory demonstrator circuits fabricated on plastic (*5*, *6*) with low-cost fabrication methods, such as ink-jet printing and a high-resolution form of rubber stamping known as microcontact printing (*7*). A photochemical patterning process has also been developed for devices that use certain types of photosensitive plastics (*8*).

Our recent work combines organic semiconductors with rubber-stamped circuit elements on thin sheets of plastic to produce high-quality, large-area circuits for displays (*9*). A typical system consists of a square array of several hundred suitably interconnected organic transistors with micrometer feature sizes distributed over areas of 6 inches by 6 inches. The circuits incorporate five layers of material, patterned in registry with one another and processed entirely outside a clean-room environment. The compatibility of the stamping method with high-speed, continuous reel-to-reel printing approaches, the large area coverage, and the good performance of the transistors are all important features of these flexible circuits.

The figure shows a photograph of the Bell Labs electronic paper display and an artist's impression of the different components of this system. It uses rubber-stamped plastic circuits and microencapsulated electrophoretic inks. The entire device is less than 1 mm thick and weighs about 20% as much as a liquid crystal display of similar size. The exploded view (not to scale) illustrates the layout of a unit cell. Each pixel is associated with an organic transistor that acts as a voltage-regulated switch to control the color of the ink.



The nuts and bolts of electronic paper. The exploded view shows the elements in a unit cell (not to scale). Arrays of rubber-stamped plastic transistors (inset on the left; blue, organic semiconductor; gold, source/drain electrodes; gray, gate electrode) control the color of a layer of microencapsulated electronic ink (inset on the right).

The ability of the stamping method to form micrometer-sized features on plastic substrates is critically important for this circuit. It enables the transistors to achieve the necessary switching speed, even with semiconductors that have modest electrical performance. Furthermore, it allows the same circuit design to be extended to high-resolution displays with large numbers of pixels. This scalability and the gradual emergence of other suitable materials and processing techniques point to a bright future for flexible electronic systems. These technologies will enable not only electronic paper displays and other applications that we can anticipate today (such as low-cost identification tags) but also completely new and unexpected devices that will change the way that we think about consumer electronics.

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PERSPECTIVES: IMMUNOLOGY

B Cell Receptor Rehabilitation—Pausing to Reflect

Leslie B. King and John G. Monroe

One of the most crucial steps during B cell development in the bone marrow is the expression of the B cell receptor for antigen (BCR). The BCR, a cell surface form of antibody, is responsible for initiating the B cell response to pathogens and other antigens. Unique antigen-specific antibodies are expressed by individual B cells after the developmentally regulated rearrangement of gene segments within the heavy and light chain loci of antibody genes. The random nature of the rearrangement, coupled with the complexity contributed by heavy and light chain pairing, creates an incredibly diverse antibody repertoire. Although such diversity allows for the immune recognition of a vast array of foreign pathogens, it concomitantly yields B cells that are potentially self-reactive. To avoid autoimmune responses elicited by activation of these cells, the immune system has two ways in which it induces tolerance to self antigens: physical elimination of self-reactive cells through apoptosis (clonal deletion) or impairment of their activity (clonal anergy). More recently, receptor editing, during which there is a secondary rearrangement of the antibody light chain locus, has been proposed as another way to eliminate autoreactive B cells (*1*–*3*). On page 1541 of this issue, Casellas *et al.* (*4*) now report that receptor editing is likely to be a major force in shaping the B cell antibody repertoire (see the figure). They show that receptor editing takes place during a 2-hour delay in B cell development and that at least 25% of pre-B cells end up expressing edited versions of their originally self-reactive antibodies.

Receptor editing provides a simple way for autoreactive B cells that have received a verdict of either death (deletion) or life imprisonment (anergy) following encounter with antigen to commute their sentence by producing a rehabilitated nonautoreactive BCR. Such a scenario is supported by a number of studies in transgenic mice. In these studies, transgenic mice were engineered so that pre-rearranged antibody heavy and light chain antigen-combining regions encoding autoreactive BCRs were "knocked in" (inserted by homologous recombination) to their respective endogenous loci, preserving the potential for secondary rearrangements (*5*, *6*). In these transgenic animals, autoreactive BCRs were edited to a much greater extent than their more innocuous counterparts. However, the involvement of

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