Moving back to the lab, the next step will be to understand in molecular detail where survival pathways and chemotherapy agents intersect. ■

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Semiconductor physics

Quick-set thin films

Mercouri G. Kanatzidis

Transistors that have active components based on thin films, rather than silicon, are attractive for many applications. The latest thin-film fabrication technique has the potential for industrial-scale production.

The original working transistor, invented at Bell Labs in the 1940s, was based on semiconducting germanium and had a junction (sandwich) configuration. But by the 1960s, this design had given way to the simpler field-effect transistor — in particular, the silicon-based MOSFET (for metal-oxide-semiconductor field-effect transistor). A typical computer processor today contains around 42 million such transistors, and demand for ever-faster computers is only increasing. As a result, the market is pushing for a downsizing of transistor technology.

However, certain applications (such as flat-panel displays) require larger-area transistors than can normally be created using silicon-based devices. Thin-film semiconductors have been explored as an alternative, although with limited success. But now it seems that the large-scale, low-cost fabrication of such devices is a step closer: on page 299 of this issue, Mitzi *et al.*[1] describe a chemical-deposition method for producing uniform films of the chalcogenides SnS_2 or $SnSe_2$ for use in thin-film transistors (TFTs). The resulting TFTs support large current densities (more than 10^5 A cm^{-2}), and mobilities greater than 10 cm^2 V^{-1} s^{-1} — almost ten times larger than achieved for semiconducting films formed using the spin-coating technique (in which a solution on a substrate is spun rapidly, causing the film to spread outwards).

In a TFT, the thin film (usually silicon) is the active current-carrying layer (Fig. 1). The film sits on a substrate, which is usually glass owing to its low cost, high optical transparency and compatibility with conventional semiconductor processing technology. Recently, however, plastic has emerged as a viable challenger because of its additional flexibility, although the development of TFT technology for use with plastic substrates is still in its infancy.

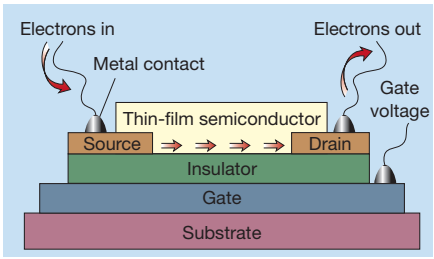

Figure 1 **Cross-section of a thin-film transistor. A voltage applied at the gate controls the flow of electrons (resistance) from the source to the drain; a positive gate voltage attracts electrons to the bottom surface of the semiconductor layer and creates a conduction channel. When a voltage difference is applied between the two connector wires, electrons enter at one end (the source) and exit at the other (the drain), resulting in a current along the channel. Mitzi *et al.*[1] have now come up with a chemical-deposition method that produces uniform films of the chalcogenide $SnSe_2$ for use in thin-film transistors.**

Transistors for high-performance display applications should have high electron mobilities, low leakage currents and low threshold voltages. But processing temperatures must also be low (below 150 °C) if the transistors are to be compatible with low-cost plastic substrate materials. So the emphasis in developing large-scale TFTs has been on low-temperature deposition and the exploration of materials other than amorphous silicon. Approaches include vacuum deposition[2] (suitable for growing ultrathin organic films and multilayer structures), solution-deposition technologies[3] (suitable for inorganic materials), and many others[4]. But these are generally not high-throughput processes. Although spin-coated semiconductor films have suffered from low mobilities[5–7], this technique shows much promise.

The attraction of using inorganic semiconductors lies in their stability, thermal robustness and high mobilities. The metal chalcogenides, for example, are excellent candidates for use in TFT technologies. They form a large class of compounds that are composed of one or more metals plus one of the chalcogen atoms such as sulphur, selenium or tellurium. Moreover, the energy required to delocalize a charge carrier (the energy gap)[8] in these materials is suitable for room-temperature devices, and can be further tuned for a given application[9].

Mitzi *et al.*[1] describe a means of creating chalcogenide active layers for TFTs through spin coating. Their continuous, uniform, ultrathin semiconducting films are only a few unit cells thick. The key to the fabrication chemistry is hydrazine (N_2H_4), which Mitzi *et al.* use as a solvent. When metal and chalcogens dissolve in hydrazine, they form chalcogenometallate solutions containing anions such as $[Sn_2S_6]^{4-}$, as well as hydrazinium cations $(N_2H_5)^+$. These solutions can be used as precursors for spin-coating thin films of the salt $(N_2H_5)_4[Sn_2S_6]$, which then decompose to the binary metal chalcogenide at low temperature. The advantage of having hydrazinium cations, and not some other organic cations[10], is that they readily and cleanly react with the counterion of $[Sn_2S_6]^{4-}$ to give continuous, crystalline semiconducting films as thin as 5 nanometres.

It is this simple chemistry that not only makes the work of Mitzi *et al.*[1] attractive, but probably technologically significant as well. Thin films produced by deposition from solution have so far been moderately successful in terms of their mobilities[11–13], but the techniques are generally not suitable for high throughput. This hydrazine-based process can be applied more generally, and the hydrazinium salts need not be isolated first — they can be made *in situ*. If the process can be optimized and scaled up, thin films for high-performance channel layers in TFTs could be fabricated with all the processing performed at 300 °C. In principle, depending on the specific metal chalcogenide involved, the films could be made at even lower temperatures.

However, the current processing temperature is too high for many applications (such as those using plastic substrates), and the mobilities achieved, although much higher than reported for other techniques, may not yet be adequate for many devices. Furthermore, the source and gate voltages of the TFTs are higher than those of typical silicon-based devices, while little is known about the yield and reproducibility of these devices. And the substrate is still silicon, not glass or plastic, which will limit the fabrication of TFTs on large-area, low-cost substrates.

So there are several factors to be considered before a new generation of optoelectronic devices based on this deposition

technology could gain a foothold, including the long-term operational and environmental stability of the devices. But, given the relative youth of this technology, and the exciting and rapid advances anticipated using chalcogenide thin films, the goal does not seem unattainable. Continued work in this area is likely to contribute to our understanding and exploitation of these exciting materials well into the next century. ■

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Cancer

Dangerous liaisons

Allan Balmain and Rosemary J. Akhurst

The cells of multicellular organisms are highly communicative and so can strongly influence one another's behaviour. One line of communication is particularly important in keeping cell growth in check.

A single cell destined to become a tissue or an organism can't go it alone in its rise to such dizzy heights. Communication, in the form of direct contacts between cells, interactions between cells and their surroundings, or the transmission of biochemical signals, is essential. Unravelling these networks of communication has provided gainful employment for biologists, geneticists and mathematicians in their quest to understand how the body forms[1]. But now cancer biologists are being drawn into a similar web of interactions between cells targeted to become tumours (usually epithelial cells) and their neighbours (stromal fibroblasts). A network of signals operates in tumours. As they describe in *Science*, Bhowmick *et al.*[2] have identified one signalling pathway — regulated by transforming growth factor β (TGF-β) — that is an important mediator of the stromal–epithelial interactions modulating the growth of solid tumours.

It has been known[3] for some years that normal stromal cells inhibit tumour growth whereas tumour-associated stromal cells stimulate it (Fig. 1). In their study, Bhowmick *et al.*[2] deleted the receptor for TGF-β — the TGF-β type II receptor — specifically in stromal cells of otherwise normal mice. This 'selective knockout' avoided killing the animals by deleting the TGF-β type II receptor in every cell type, completely inhibiting signalling through this pathway in the stroma of several tissues. Surprisingly, although the deletion occurs in the skin, oesophagus, kidney, liver and lung, mice were born normally, and these tissues showed no observable adverse effects.

Not everything, however, escaped unscathed. Prostate tissue underwent increased stromal-cell division, growing excessively by the time the animals were three weeks old. This, in turn, stimulated the epithelial cells of the prostate to divide and form lesions that resembled prostatic intraepithelial neoplasia, a probable forerunner of prostate cancer. The stromal-cell population in the animals' forestomach also proliferated more rapidly, in this case spurring the expansion of the epithelial population so that an invasive form of cancer occurred that killed the mice by the time they were seven weeks old. So not only does abrogation of TGF-β signalling in the stromal fibroblasts cause them to proliferate, but the ensuing perturbed communication with the epithelial cells causes dysregulated cell division, indirectly leading to cancerous growth.

What causes this? Perhaps the stromal cells that cannot respond to TGF-β instead release other factors, or greater amounts of certain factors than do normal stromal cells? Bhowmick *et al.*[2] suggest that it might be due to another growth factor, hepatocyte growth factor (HGF), acting through its receptor c-Met (Fig. 1). The HGF–c-Met regulatory system is important in proliferation, cell migration and metastasis — the movement of cancer cells to other parts of the body to establish more tumours[4]. Impressively, fibroblasts from both the forestomach and prostate tissues of the knockout mice secreted at least three times as much HGF as their normal counterparts, and c-Met was simultaneously activated in the proliferating epithelial cells of the forestomach tumours.

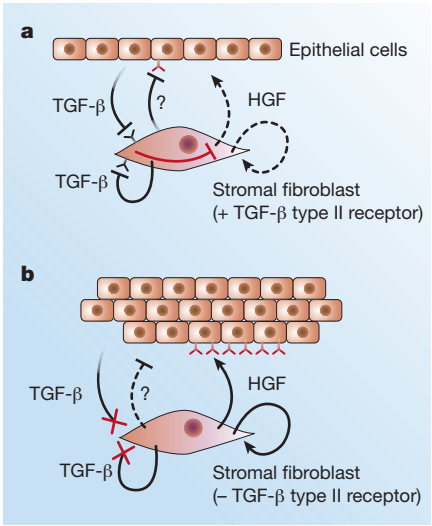

Figure 1 **Cellular relationships.** a, **Normal communications between epithelial cells and their fibroblast neighbours. Both epithelial cells and fibroblasts secrete transforming growth factor β (TGF-β), which suppresses growth. Stromal fibroblasts might also secrete other factors that inhibit epithelial-cell growth (denoted by ?). A small amount of hepatocyte growth factor (HGF; its receptor is c-Met) secreted by the stroma inhibits stromal-cell growth and also that of epithelial cells.** b, **Perturbed signalling in the absence of the receptor for TGF-β, the TGF-β type II receptor. Inhibition of TGF-β signalling in stromal cells prevents growth-inhibitory responses to TGF-β and stimulates the stroma to release higher levels of HGF, a positive growth and metastatic factor. The production of other growth-inhibitory factors (?) might be reduced in response to inhibition of TGF-β signalling. TGF-β receptors are shown in black, c-Met receptors in red.**

These data are consistent with previous reports that TGF-β normally inhibits HGF synthesis in stromal cells[5]. But they don't reflect the situation in advanced skin cancer, in which tumour-derived TGF-β induces adjacent stromal cells to produce HGF[6].

The study by Bhowmick and colleagues has uncovered insights into cellular liaisons within tissues that should benefit cancer researchers and developmental biologists alike. But several issues raised by the findings must first be resolved. The cells of most solid tumours secrete large amounts of TGF-β, but are insensitive to its growth-inhibitory effects. This means either that components of this signalling pathway have mutated or, as is more common, that the growth response has been reduced while the ability to migrate, invade and metastasize in response to TGF-β is retained. How, then, do stromal cells normally escape the growth-inhibitory effects of overexpressed TGF-β and become willing partners in fostering epithelial tumour progression? Possible answers are genetic changes, or changes in gene expression that occur without altering the DNA sequence.