have already demonstrated that these dense nanowire arrays can be interconnected with reliable metal contacts. Second, it is possible to transfer monolayers, layer by layer, to form parallel and crossed-nanowire structures that could serve as optoelectronic components.

Just as the log drive can extend over many miles of river, the Langmuir–Blodgett technique can be used to assemble large areas of nanowire monolayers on a water surface — up to 20 cm^2 is easily achieved. The monolayer area is limited only by the number of the nanowires dispersed on the trough surface. This type of large-scale nanowire assembly is unprecedented, and could be applied to many other one-dimensional nanostructures, including carbon nanotubes, for example. The feasibility of transferring multiple layers of metal or semiconductor nanowires onto flexible substrates also points to new directions for flexible electronics and optoelectronics.

Transforming spaghetti-like, tangled nanowires into an ordered, large-area array by the Langmuir–Blodgett technique is a remarkable feat. As Whang *et al.*[1] point out, this process offers a flexible pathway for the step-by-step assembly of virtually any nanowire material into the highly integrated and hierarchically organized nanodevices that are needed for a broad range of functional nanosystems. But this is not the end of the story. For nanostructured technology to be competitive, being able to create high-density arrays is not enough: how to address individual elements in a high-density array and how to achieve precise layer-to-layer registration for vertical integration are just two of the many challenges still ahead. ■

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Molecular biology

MicroRNA is here to stay

Philip N. Benfey

A form of gene regulation that uses small RNA molecules to bind to longer RNAs was first described over a decade ago, but was thought to be of little significance in controlling cellular processes. No longer.

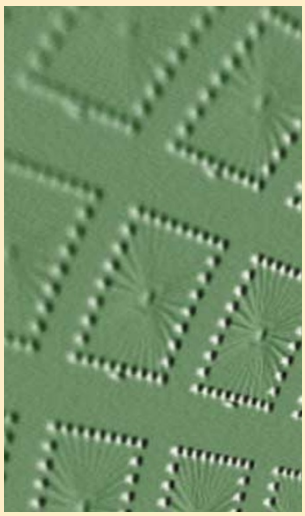
The first glimpse of the wave was more than a decade ago, when a strange form of gene regulation was described that involved the binding of one RNA molecule to another[1]. Then last year, with reports that there are hundreds of small RNAs in the genome[2–5], it came into view. There was the possibility that a whole layer of gene regulation involving very small RNA molecules called microRNAs had been overlooked for 40 years. But still there were doubts as to the importance of microRNAs — the wave might yet turn out to be scarcely a ripple, let alone a tsunami. With the description by Palatnik *et al.* of the role of microRNAs in controlling plant

Electronics

Nanotechnology goes large

Discovering new ways of making and manipulating materials at nanometre scales should help to maintain the computer industry's relentless drive towards ever greater miniaturization and performance. But in this issue, Xiangfeng Duan and colleagues show that, in addition to allowing the development of high-performance nanoelectronics, these techniques may also be useful for making flexible electronics over large areas and at low cost (*Nature* **425,** 274–278; 2003).

At present, making microelectronics involves a lot of waste. More than 95% of the bulk of the precious silicon wafers from which most microchips are made serves no other purpose than as a mechanical support for the circuitry patterned into its surface. For laptop computers, digital cameras, portable music players and other high-value gadgets, the cost associated with such waste is easily absorbed into the price. But for products such as 'smart clothing' or electronic paper — which involve higher volumes, large areas and more modest price tags — this cost becomes prohibitive. Moreover, the high temperatures required to grow crystalline silicon (in excess of 1,400 °C) make many such products difficult to produce at any price. But by growing only as much semiconductor material as is needed for electronic circuitry on the surface of an inexpensive substrate material such as glass or plastic (see picture), significant reductions in cost can be achieved.



X. DUAN, NANOSYS INC.

Commercially, large-area electronic devices are based on either amorphous silicon (used in most LCD displays) or, more recently, organic semiconductors (as in the display on James Bond's electric shaver). The performance of these materials, however, is poor compared to conventional crystalline semiconductors, and is always likely to be so. But by using newly developed techniques for growing crystalline semiconductors in the form of tiny nanometre-diameter wires and ribbons — techniques that are currently being pursued for making nanoscale devices (see "Wires on water" by Peidong Yang, above) — Duan *et al.* show that high-performance, low-cost macroelectronics could be just around the corner.

By aligning silicon nanowires or cadmium-sulphide nanoribbons between metal electrodes, the authors can create field-effect transistors — the fundamental building-blocks of modern electronic circuitry — with characteristics better than those of similar amorphous silicon or organic semiconductor devices, and approaching those of polycrystalline silicon devices. By increasing the density of wires and ribbons between the metal electrodes, Duan *et al.* expect soon to be able to improve this performance even further. And with the recent advent of nanowires made from high-mobility materials such as indium phosphide and indium arsenide, such devices could in future exceed the performance of crystalline silicon devices. **Ed Gerstner**

development (page 257 of this issue[6]), and other new publications reporting important functions in animals[7–9], the wave looks very real — and big.

In the beginning there was the view that DNA makes RNA makes protein, and life was simple and good. Other functions for RNA were discovered. But they were mostly structural, such as being a part of the ribosome, the cellular site of protein manufacture. Then in 1993, while studying mutations that changed the timing of developmental events in the worm *Caenorhabditis elegans*, Victor Ambros made a startling discovery[1]. A mutation that caused an increase in the translation of RNA to protein was found to be in a second, very small RNA molecule. The small RNA was shown to bind through base pairing to one end of an RNA that controlled the worm's ability to develop properly. The binding of the small RNA resulted in a block to translation of the messenger RNA. Seven years later, a second case of a small RNA used to regulate the translation of a messenger RNA was reported[10]. However, the small RNA was again found in worms and was controlling a similar developmental process. It was beginning to look as if this was just another baroque facet of evolution — a form of regulation that was highly specialized for one organism and one function.

What rescued microRNAs from neglect was genome sequencing. Several groups started to look for sequences within the genome that were transcribed into RNA but the RNAs were not used to make proteins. They combined bioinformatics searches with sophisticated procedures that allowed them to isolate only small RNAs. What they found was that in organisms ranging from plants to man there were hundreds of small RNAs (18–25 nucleotides) that were actively transcribed and highly conserved between related species[2,4,5].

The next task was to determine what these microRNAs were doing. Last year, two groups published the dramatic findings that many of the apparent targets of plant microRNAs are transcription factors implicated in the control of developmental processes[2,4]. Transcription factors are proteins that control gene activity. So the findings led to speculation that a primary role for microRNAs in plants is to regulate gene expression after a cell division event that leads to the formation of two different cell types. But to identify putative targets through bioinformatics is one thing. To prove that microRNAs are really regulating a developmental process is quite another.

Palatnik *et al.*[6] have done just that, although it was not the original intent of their project. They were screening a collection of mutants of the plant *Arabidopsis*, made by randomly inserting a piece of DNA into the genome that increases transcription of neighbouring genes. They found several mutations that caused leaves to curl rather than lie flat. When they sequenced the region of the genome near the inserted DNA they discovered what appeared to be a gene encoding a microRNA named *JAW*. To identify possible targets of the microRNA, they used microarrays to compare the global expression profile of the *jaw* mutants with that of wild-type plants. Among the RNAs with the greatest differences were four members of the TCP class of transcription factors, which had been shown to control leaf curvature in snapdragon. Alignment of the JAW microRNA with the TCP RNAs showed near perfect complementarity (Fig. 1).

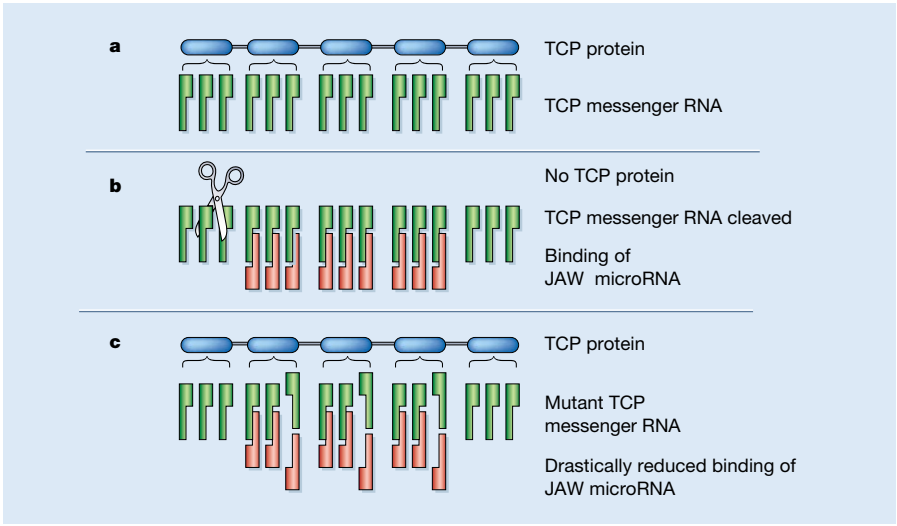


Figure 1 **MicroRNAs in action. In the early days of molecular biology, RNA was known only as a way of transferring information from DNA to protein. But microRNAs do not make protein and they prevent protein from being made when they bind to messenger RNAs.** a, **When unbound, messenger RNA of the TCP gene-transcription factors makes protein. Each set of three nucleotides (green) is a codon for a specific amino acid (blue).** b, **The JAW microRNA (red) binds by complementary base pairing to the TCP messenger RNA and leads to cleavage of the messenger RNA, thus preventing protein from being made.** c, **Palatnik *et al.*[6] changed the third nucleotide in the codons of the TCP messenger RNA. This drastically reduces the ability of the JAW microRNA to bind to its target, but does not change the protein that is made. Introducing the gene for this modified TCP messenger RNA into wild-type plants resulted in defective leaf development, indicating that microRNAs are controlling the process.**

A series of elegant experiments showed that TCP gene function was indeed controlled by the JAW microRNA. The TCP sequence was modified so that the JAW microRNA could no longer bind while the protein made from the TCP RNA was not affected (Fig. 1). Introduction of this mutant form of the gene into wild-type plants resulted in severe developmental defects. That is, the microRNA could not carry out its job, which was evidently to control the availability of TCP protein.

Further evidence that the critical control point was exercised by microRNAs came from overexpressing a normal TCP RNA. For many transcription factors, overexpression of their RNA is like forcing too much electricity through a circuit. But overexpression of the TCP RNA caused no obvious defects. The same construct introduced into the *jaw* mutant was able to partially rescue the leaf-curling defect. The likely explanation is that in the *jaw* mutant, the inserted DNA causes too much JAW microRNA to be produced and it is no longer restricted to certain tissues. Making more of the target RNA sops up the excess JAW microRNA.

The paper by Palatnik *et al.*[6] provides one of the most compelling cases that the newly discovered microRNAs have an important role in controlling development. Other recently published results highlight the involvement of microRNAs in regulating processes ranging from cell proliferation and programmed cell death in flies[7] to neuronal differentiation in humans[8]. Among the many unanswered questions that surround microRNA function a central one is, what controls microRNA expression? Is there still another level of regulation that has been overlooked — another wave just beyond the horizon? ■

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