Semiconductor technology

Negatively successful

Ananth Dodabalapur

Organic semiconducting polymers are promising electronic materials, but for full versatility they need to conduct negative as well as positive charge. A step towards that goal has now been taken.

Electronic devices based on organic materials are gradually becoming a mainstay of semiconductor technology, and are already used, for example, in flexible displays. However, a few hurdles remain before a breakthrough in practical applications can occur. One nagging problem is that organic transistors are so far only efficient at carrying electronic current via positive charge carriers (holes). To realize a complete electronic circuit based on organic polymers, analogous to conventional silicon chips, devices must also be able to carry negative charge (electrons). On page 194 of this issue, Chua *et al.*[1] demonstrate a design principle that would turn any organic field-effect transistor (FET) into one that efficiently carries negative charge.

The past decade has seen many efforts to develop so-called 'n-channel' organic FETs, in which electrons, rather than holes, are the charge carriers[2–6]. This work is not aimed solely at immediate applications, but also at achieving a better understanding of the relation between materials and device performance.

The guiding principle in the design of semiconductor and electrode materials for n-channel FETs has been to optimize energy levels so as to achieve high electron mobility. But compared with 'p-channel' FETs (where the charge carriers are holes), such devices are generally found to be more sensitive to moisture and oxygen. To combat this problem, organic materials have been developed to have high electron affinity, which means that they strongly attract electrons and are not easily oxidized. However, electron affinity cannot be too high, or the material will become prone to unwanted doping, which is detrimental to the performance of a transistor.

An example of an organic semiconductor material based on this design principle of optimizing energy levels is a pair of materials known as F_{15}NTCDI and H_{15}NTCDI. Although the fluorine-free material has good electron mobility, transistors made with just this compound operate only under vacuum, where the effects of moisture and oxygen are much reduced. The fluorine-containing compound, on the other hand, has a higher electron affinity and can operate in air[2].

Ultimately, materials are needed that are 'ambipolar' — that is, that can be used to create both n-channel and p-channel FETs. Until now, materials for making organic and polymer transistors have generally been lumped into one of the two categories, either n-channel or p-channel[7]. Traditional organic FET materials, such as pentacene, α-sexithiophene and polythiophenes, are known as p-channel materials and have been difficult to coerce into taking on n-channel behaviour.

However, experimental results suggest that the difficulty in observing efficient transport of electrons in an organic FET is an extrinsic effect caused by factors other than the organic semiconductor material itself. This conclusion would be in tune with the observation that, in purified single crystals of small organic semiconducting molecules, both electrons and holes move with roughly comparable mobilities.

For example, a traditional p-channel FET — based on pentacene — has been converted into an n-channel device by inserting calcium at the interface between pentacene and the thin insulating layer used in transistors[8]. The conclusion was that electrons from the calcium atoms fill up a large number of the 'traps' in the insulator that inhibit electron transport. Removal of these traps results in efficient n-channel behaviour.

Chua *et al.*[1] make a convincing case that the trapping of electrons at the insulator–

Structural biology

Methanol maker

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Methanol could become an alternative source of energy, possibly replacing the less environmentally friendly combustion of coal and petroleum. The right-hand part of the picture shows burning methanol, which combusts much more cleanly than gasoline (on the left). Methanol can be produced by oxidizing methane, the main component of natural gas. But there are no catalysts that can efficiently perform this chemical reaction on an industrial scale at low temperature.

Several natural enzymes can carry out the reaction, however. Elsewhere in this issue (*Nature* **434,** 177–182; 2005), Raquel L. Lieberman and Amy C. Rosenzweig report the X-ray crystal structure of one of them — particulate methane monooxygenase (pMMO) from the bacterium *Methylococcus capsulatus*. The structure helps to settle years of controversy by revealing that the protein is a cylindrical trimer, with three metal centres in each subunit. Two of the centres contain copper; one centre is mononuclear (containing a single copper ion), whereas the other is dinuclear (with two copper ions in close proximity). The other metal centre contains a zinc atom, which Lieberman and Rosenzweig believe came from the buffer used to crystallize the protein; they think that the natural protein contains either copper or iron at this centre.

It is still unclear which of the metal centres is the catalytic site — it could be any of them, say the authors. However, clues to the answer might come from structural similarities between a subunit of pMMO and cytochrome *c* oxidase subunit II, the terminal enzyme in the respiratory chain, which contains a dinuclear copper centre involved in electron transfer. The dinuclear copper centre of pMMO could likewise be responsible for shuttling electrons to the catalytic site, which may be the nearby mononuclear copper centre.

The structure also shows which amino-acid side chains are associated with each metal ion. But much remains to be done. For example, the resolution of the structure is not high enough to determine whether the metal centres contain additional ligands, such as water, that could be functionally important. Nonetheless, the new work is a step along the way to finding out how pMMO works, and towards the long-term goal of developing small-molecule catalysts that might replicate methane-to-methanol conversion in an industrial setting. **Joshua Finkelstein**

semiconductor interface is indeed the culprit, and they relate this trapping to electronegative hydroxyl (OH) groups in the insulator material. When they use materials that are free of hydroxyl groups, uninhibited electron transport is indeed observed. By using bisbenzocyclobutene as the insulator, for example, organic polymer FETs based on materials such as poly(fluorine-*alt*-bithiophene) and poly(fluorine-*alt*-benzothiadiazole) are shown to exhibit n-channel behaviour.

Chua *et al.* conclude that if the trapping of electrons by electronegative groups in the insulating layer could be avoided, then n-channel behaviour would be seen in a broad range of semiconductors. Their most convincing example is that of polythiophene, which is relatively prone to oxidization and therefore normally more difficult to use in n-channel FETs.

Of course, it remains to be seen whether, on prolonged exposure of the device to ambient conditions, the effects of atmospheric moisture and oxygen would negate those of a hydroxyl-free insulator material. But the finding is nevertheless a remarkable result and a major step forward in our understanding of the design principles of materials and devices for n-channel organic transistors.

Chua and colleagues' work also explains why some semiconductors transport both electrons and holes when used as an active layer in light-emitting diodes — where there are no insulating interfaces — but exhibit only n-channel behaviour in FETs[9]. The implication is that such materials, which readily exhibit n-channel behaviour but not p-channel behaviour, could also be made ambipolar by identifying what causes hole trapping at the semiconductor–insulator interface and eliminating it.

Another area that will benefit greatly from this study is the work on ambipolar organic FETs with a view to making efficient light-emitting transistors[10]. A wider choice of materials for this type of research will become available once electron trapping is eliminated or greatly reduced. ■

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Developmental biology

Sperm–egg fusion unscrambled

Richard Schultz and Carmen Williams

The identity of the sperm molecules that are involved in fusion with an egg's membrane has eluded biologists. Will Izumo, a protein named after the Japanese shrine to marriage, bring harmony to the field?

In the life history of sexually reproducing organisms, fertilization is a defining event. In mammals, sperm and egg have a limited lifespan once present in the female reproductive tract. Fertilization 'rescues' these gametes in a multi-step process that ultimately results in the fusion of their membranes and formation of a zygote. Despite the importance of the interactions that lead to zygote formation — and despite decades of research — the molecular basis for sperm–egg fusion has remained poorly understood, and the field is littered with the carnage of erstwhile molecular candidates. The latest discovery is of a sperm-specific protein called Izumo, and the evidence that it is required for fusion, presented by Okabe and colleagues[1] on page 234 of this issue, is compelling.

The steps involved in sperm–egg fusion are illustrated in Figure 1. Briefly, the cumulus cells that surround an ovulated egg secrete a matrix containing hyaluronic acid. A sperm must first pass through this matrix, and then interact with the egg's coat (the zona pellucida); this stimulates secretion of the contents of the sperm's acrosome — an intracellular sack of molecules necessary for sperm to penetrate the zona pellucida. Once through this coat, the sperm gains access to the perivitelline space, and binds to the egg's plasma membrane. Sperm and egg membranes then fuse.

Historically, antibodies have been used to identify proteins from the surface of mouse sperm that are involved in fertilization. In this way, PH-20 was identified as an enzyme that helps sperm to pass through the hyaluronic-acid-containing matrix[2]. The same approach identified the fertilin αβ protein as a candidate for mediating sperm–egg fusion — an exciting finding because of the structural nature of the fertilins. These proteins were the founding members of the ADAM (for 'a disintegrin and metalloprotease') superfamily[3]. Fertilin α and β each contain a disintegrin domain, which might mediate cell–cell adhesion by interacting with an egg integrin protein; fertilin α also contains a domain related to that of viral fusion peptides, which might mediate sperm–egg membrane fusion.

Unfortunately, however, later work did not support a role for fertilin α in membrane fusion, and sperm derived from fertilin-β-deficient mice can still fertilize eggs. Furthermore, wild-type sperm can bind to and fuse with eggs deficient in each of the integrins that are likely to interact with ADAM disintegrin domains. These results deflated the previous excitement and left the field in a profound state of uncertainty.

The results described in this issue by Okabe and colleagues[1] should rekindle a sense of vitality in this area of research. Okabe and colleagues[4] reported 18 years ago that a particular antibody, OBF13, recognizes a molecule on the sperm head that is exposed following the acrosome reaction. A later study[5] indicated that although this antibody did not inhibit sperm–egg binding, it did prevent fertilization *in vitro*, hinting that the protein it binds is involved in fusion. Now, Okabe and colleagues[1] have used liquid chromatography tandem mass spectrometry to identify this protein, and have named it Izumo. The protein sequence indicates that Izumo (and its human counterpart) is a member of the immunoglobulin superfamily, and other experiments show it to be sperm-specific.

The authors used a knockout approach to assess a role for Izumo in fertilization. Females lacking the protein were phenotypically normal and fertile. In contrast, although Izumo-deficient males were phenotypically normal — and their sperm were also normal in morphology and motility — they were completely infertile. The Izumo-deficient sperm could reach eggs *in vivo*. They showed no reduction in their ability to bind to and penetrate the zona pellucida *in vitro*. And, once in the perivitelline space, they could bind to the egg plasma membrane. But not a single Izumo-deficient sperm was observed to fuse with the egg membrane. The authors ascribe this inability directly to the lack of Izumo, because expressing this protein in Izumo-deficient males restored fertility. Finally, they found that bypassing membrane fusion by injecting Izumo-deficient sperm into eggs resulted in activation of the eggs and development to term. These results, and more, strongly suggest that the sole function of Izumo is in sperm–egg fusion.

So, how does Izumo promote membrane fusion? Because its extracellular region lacks sequences like those found in viral fusion peptides, it is unlikely that Izumo is inherently fusogenic. A more likely possibility is that it serves as an adhesion molecule, given that it has an immunoglobulin-like domain — a well-defined domain for mediating cell–cell adhesion (see, for example, ref. 6). In contrast to most members of the