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damage, including bleeding and infiltration of immune cells, at times well after the peak of virus replication. A whole-genome analysis of gene expression — the first in monkeys infected with the 1918 virus — showed that the virus triggered aberrantly high and sustained expression of genes encoding many proteins involved in the innate immune response, including proinflammatory cytokines and chemokines. So Kobasa *et al.*[3] propose that an aberrant innate immune response to the 1918 influenza virus could be responsible for the rapid, severe outcome of the infection (Fig. 1). Their data suggest that persistent elevation of inflammatory-response genes could account for the massive inflammation and infiltration of immune cells observed in the respiratory tract of animals infected with the 1918 virus.

Notably, infection with contemporary influenza virus triggered robust expression of genes encoding several α-interferon subtypes and of interferon-stimulated genes with known antiviral properties, and this expression was associated with the comparative mildness of the disease. By contrast, the 1918 virus induced only low and selective expression of genes encoding α-interferon subtypes and differential expression of many interferon-stimulated genes — including one that encodes a protein called RIG-I. Contemporary influenza A virus triggers innate immune defences in part through RIG-I, which regulates the expression of other immune and inflammation genes[6]. But tissue infected with the 1918 virus showed reduced RIG-I expression compared with tissue infected with the contemporary virus. Although these observations may conceptually link RIG-I activity to intracellular pathways that would normally induce the production of interleukins and chemoattractants to clear the virus, the study lacks the biochemical data that are essential for defining such connections.

Kobasa *et al.*[3] demonstrate the power of functional genomics in untangling the complexities of virus–host interactions and viral pathogenesis. Their gene-expression profile analyses suggest that the 1918 virus triggers innate immune signalling processes that possess altered kinetics relative to the contemporary influenza A virus, and/or that the 1918 virus may selectively attenuate the expression of specific innate-response genes. The authors did not, however, analyse gene expression during the important early time course of these events (the first hours and days of infection), so determining the exact mechanisms regulating gene expression will take further study. But it is worth mentioning one possible candidate molecule: the nonstructural-1 (NS1) protein of the influenza A virus can suppress innate immunity by disrupting the induction of α/β-interferon and/or altering the maturation of host-cell RNA[7,8]. Of course, NS1 does not work alone[9], and virulence attributed to pandemic influenza requires many viral components in a unique assemblage of genes[1,2].

The work of Kobasa *et al.* substantiates the findings of Kash *et al.*[10], who showed in mice that the 1918 virus triggered a vigorous innate immune response that was linked to fatalities. Although the mechanisms of tissue destruction were not addressed in either study, the work clearly demonstrates the vital function of early innate immune defences in controlling the virus. It seems that the pandemic 1918 virus had a genetic composition and rapid replication kinetics that may have resulted in an excessively vigorous innate immune and inflammatory response that contributed to severe tissue damage, disease and death.

These conclusions correspond to the striking epidemiological data showing that, unlike contemporary influenza strains, which typically affect the very young and the elderly most severely, the 1918 influenza pandemic was mostly fatal in young adults, who generally possess more robust immune systems[1]. Unveiling the contribution of an aberrant host response to the pathogenesis of the 1918 virus is just the beginning of efforts to understand the disease mechanisms underlying the 1918 pandemic and new virulent strains of influenza virus. The emergence of the H5N1 avian influenza or 'bird flu' virus, and its transfer to the human population, are real and continuing threats[1] that underscore the importance of the current study and of characterizing highly pathogenic forms of flu virus. A better understanding of the origin, transmission and virulence of pandemic influenza viruses, and their interactions with host immune processes, will assist our preparation against future and possibly deadly influenza pandemics. ■

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SEMICONDUCTOR ELECTRONICS

Trapped fast at the gate

Gerwin Gelinck

The speed record for programming organic transistor memory has been shattered. Work is needed on the stability of the memory storage, but it's a promising step towards some novel technological applications.

The advent of non-volatile flash memory — semiconductor memory that does not lose its data when the power is turned off — revolutionized consumer electronics. It is now used to store the numbers in mobile phones, the pictures taken with digital cameras, and the music tracks in MP3 players. Similar types of memory based on organic semiconductors, rather than traditional silicon-based semiconductors, would make possible entirely new concepts: intelligent food packaging, for instance, that could be used by retailers to control their inventories and to alert consumers when the food is getting close to its 'use-by' date. Writing in *Advanced Materials*, Baeg *et al.*[1] describe an organic thin-film memory transistor that brings such intriguing possibilities a little closer.

Two particular advantages of organic thin-film transistors over solid-state transistors are that they are simpler to make, and can be fabricated on thin, flexible plastic substrates. They could thus form the backbone of low-cost microelectronics ranging from radio-frequency identification tags to flexible, large-area active-matrix displays[2]. Many of these applications require non-volatile (stable) data storage, preferably with memory elements that can be programmed, erased and read electrically. Baeg and colleagues' transistor[1] not only fulfils these requirements, but can also, owing to its similar architecture, be simply integrated into existing technology based on organic transistors.

In order to function as a memory, a device must be observed in two (or more) different states. In flash memories, this is achieved by introducing a second 'floating gate' to the silicon transistor between the normal control gate, which regulates the flow of current through the transistor, and the semiconducting substrate (Fig. 1a). This floating gate is insulated all around by an oxide layer. A high-voltage pulse applied to the control gate places charge on the floating gate, where it becomes trapped. This partially cancels out the electric field coming from the control gate, and so modifies the threshold voltage of the transistor — that is, the voltage required before it lets current flow. Thus, when the transistor is 'read' by placing a specific voltage on the control gate, electrical current will either flow or not flow, depending on the threshold voltage, and so the number of electrons on the floating gate. The resulting

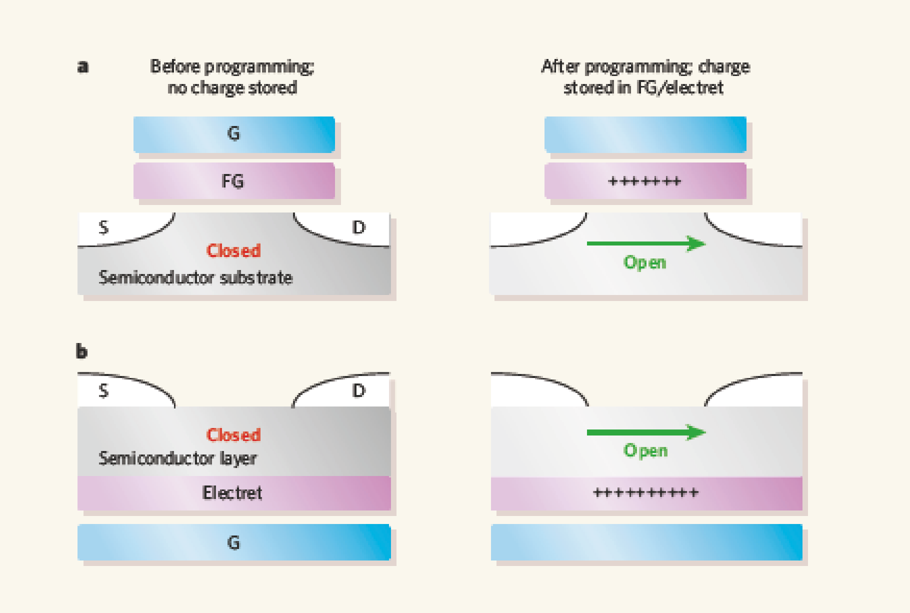

Figure 1 | Methods against memory loss. The basic transistor is a device in which a small voltage applied at the control gate (G) modulates a much larger current flow from source (S) to drain (D) through a semiconductor substrate. **a**, In flash memories, an amount of charge is trapped on a floating gate (FG) that modifies the control voltage required for current to flow from S to D. Whether current flows or not defines a boolean '1' or '0'. The memory of this state persists as long as the charge remains trapped on the floating gate. **b**, In Baeg and colleagues' organic device[1], the same principle is used, but the charge is trapped locally on a thin 'electret' of chargeable polymer, rather than on an isolated floating gate.

current level flowing through the transistor can be used to define boolean '0' and '1' memory states. The charge trapped on the floating gate persists long after all voltages are removed: the information is thus retained after power shutdown, and the transistor functions as a non-volatile memory device.

The non-volatile memory technology developed by Baeg *et al.*[1] takes a slightly different approach (Fig. 1b). Instead of charge being trapped on a floating gate, it is trapped locally on a thin layer of a chargeable polymer. This 'electret' is inserted between the insulating material (silicon dioxide) that makes up the gate and the organic semiconductor (which is pentacene, $C_{22}H_{14}$). When a high-voltage pulse is applied to this electret, it charges up. Applying a reverse voltage pulse either decharges it, restoring the initial state, or charges it to the opposite polarity. The trapped charge imposes an added voltage on the threshold gate voltage, as a floating gate does in a flash memory. This too can be sensed and translated into '1's and '0's, reproducing the stored data, by measuring the current flowing through the transistor.

Memory based on such organic field-effect transistors (OFETs) has been investigated before[3,4], but Baeg *et al.*[1] are the first to report programming speeds of around 1 microsecond — a million times faster than the previous best time of around a second. That marks a decisive step towards making organic memory technology fit for technological purposes.

The new speed record is the result of fast and efficient charge transfer from the organic semiconductor into the polymer electret by means of the electric gate field. The gate field lowers the energy barrier at the interface of the semiconductor and the electret, and so facilitates charge transfer. Once transferred, most of the charge is trapped deeply in the electret. This model explains Baeg and colleagues' most important observations: a critical gate field, caused by the energy barrier, for transfer and trapping of the charges; the lowering of this critical field when the device is illuminated with visible light; a long retention time of the order of hours in the dark; and a decrease of the retention time upon illumination.

These observations also indicate moot points. Can these devices reach data retention times necessary for practical applications — typically years for non-volatile memory? Furthermore, can the device be scaled down to more practical voltages — to 10 V from the 100 V used in the present work — without sacrificing device speed and stability? Such questions remain unanswered, but these encouraging results will without doubt spur intensive investigations into this approach.

The relevance of these results could also go beyond the scope of just memory. Baeg and colleagues[1] aim to produce non-volatile memories that exploit charge trapping and storage, but others are concerned with the converse problem: eliminating charge trapping as much as possible where it gives rise to undesired shifts in threshold voltages that can suppress 'n-channel' (electron) mobility[5] in OFETs, and limit the operational lifetime of 'p-type' (electron-hole-based) logic circuitry[6]. Whatever the intent, all will benefit from a thorough understanding of

50 & 100 YEARS AGO

50 YEARS AGO

Sir Charles Darwin writes: "The first estimate of Avogadro's number is due to Maxwell himself", and expresses his astonishment that Maxwell "should have published a fact of such tremendous importance in a manner that cannot have drawn much attention to it"... The reason for Maxwell's choice seems to have been that he did not claim to communicate anything fundamentally new, but only to discuss a line of reasoning which Loschmidt had published eight years earlier in the *Proceedings* of the Vienna Academy... It is somewhat surprising that Loschmidt's brilliant achievement has been overlooked so frequently, in spite of Maxwell's full acknowledgement... Avogadro did not even know the order of magnitude of this figure approximately; he died nine years before Loschmidt's paper appeared. F. A. Paneth

I must plead guilty to the charge of not having made a very deep search of the older literature in connexion with the evaluation of 'Avogadro's Number'... I am grateful to Prof. Paneth for putting this matter right. C. G. Darwin

From *Nature* 19 January 1957.

100 YEARS AGO

The Future in America — a Search after Realities. By H. G. Wells — There has always been in America a wide-spread contempt, not for the law, but for abstract justice, so that even well-minded, influential people do not set themselves to remedy obvious wrong when by doing so they might hurt themselves or their party in the eyes of multitudes of base and busy, greedy and childish, malevolent and ignorant voters. The unfairness of the southerner to the negro is no longer confined to the south, and the crimes of a few negroes exasperate white people so much that they forget the kindly ways of the average man of colour, and thus the negro question is becoming more complex.

From *Nature* 17 January 1907.

charge-trapping effects at the crucial interface between a semiconductor and its gate.

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CLIMATE CHANGE

Lessons from a distant monsoon

Jonathan T. Overpeck and Julia E. Cole

The burden of global warming falls most heavily on the developing world. A connection forged between the Indian Ocean climate, Asian monsoons and drought in Indonesia makes for an especially bleak outlook for that nation.

As Earth's climate continues to warm, understanding the dimensions of our vulnerability to present and future changes is crucial if we are to plan and adapt. Studies of palaeoclimate have an important role here in helping us to uncover the full range of past climate variability, and so avoid future surprises. On page 299 of this issue, Abram *et al.*[1] present a study of past climate change in Indonesia that expands our view of the pivotal climatological influences in that region to include a geographically distant player: the Asian monsoon.

Indonesia's climate is known to vary significantly from year to year as a result of the El Niño/Southern Oscillation (ENSO) system. This system is associated with changes in sea surface temperature and atmospheric pressure across the tropical Pacific. When the central tropical Pacific to the east of Indonesia is warm (an El Niño phase), the normally abundant rainfall in Indonesia moves eastward, leaving much of the island nation in drought. In the west of the country, drought is also brought about by another coupled oscillation in ocean–atmosphere conditions, the 'Indian Ocean Dipole', as a result of cool sea surface temperatures off Sumatra, the most westerly of Indonesia's principal islands.

Abram and colleagues[1] exploit the fact that climate information is preserved in the geochemistry of huge, rapidly growing corals off Sumatra to study past dipole events in the Indian Ocean. Different aspects of coral geochemistry reflect variations in temperature and in the hydrological balance (the difference between levels of precipitation and evaporation). By analysing several geochemical tracers — oxygen isotopic ratios and the ratio of strontium to calcium — in annually banded coral skeletons, the authors can reconstruct month-by-month changes in temperature and drought. Using fossil corals from the mid-Holocene (between around 6,500 and 4,000 years ago), when the Asian monsoon was stronger and ENSO seemingly weaker than today, they demonstrate that the cool ocean temperatures persisted longer — for five months, instead of three — and were accompanied by longer droughts than has been the case in modern times.

Results of climate simulations for 6,000 years ago agree with these observations and suggest a mechanism for the change. First, a stronger Asian monsoon generates anomalies in the easterly winds that would cool the eastern Indian Ocean, predisposing cooler, deep-ocean water in this area to move upward earlier during dipole events. Cooler sea surface temperatures would lead to anomalous downward movement and outflow of air from the region. The resultant weakening of the degree to which moist air converges, together with the atmospheric vertical motion, would result in reduced precipitation, and drought over adjoining land areas.

But what about ENSO? During El Niño conditions, the eastward migration of rainfall and warm ocean temperatures in the tropical Pacific lead to drought in Indonesia. But it has been suggested[2,3] that the mid-Holocene experienced background conditions that may have more closely resembled La Niña conditions. La Niña brings cooler temperatures to the central tropical Pacific, and Indonesia generally receives enhanced rainfall during these periods. So why were droughts more prominent during the mid-Holocene? The implication of Abram and colleagues' work[1] is that the Asian monsoon trumps ENSO and generates prolonged droughts in Indonesia through its influence on the Indian Ocean Dipole. Whether the more frequent droughts associated with interannual variations in ENSO are similarly affected by a stronger monsoon remains unexplored.

The implications of this study for future climate conditions are sobering. If the consensus holds true that the Asian monsoon will intensify with climate warming, Indonesia can expect more frequent and longer droughts in the future through the coupling of the monsoon with sea temperatures in the eastern Indian Ocean. Rural livelihoods and natural resources will thus be at greater risk as drought undercuts regional food supplies and stokes wildfires that also generate exceedingly poor air quality in the region (Fig. 1). Longer droughts will have many additional social and economic consequences, for example on food supply, health and hydropower. Indonesia is also a pivotal

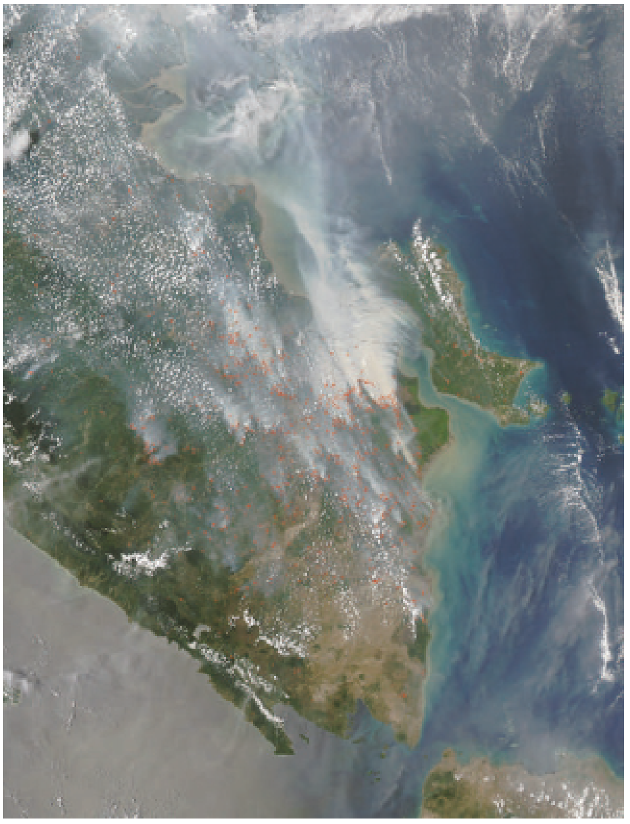

Figure 1 | Indonesian summer. Smoke from wildfires on Sumatra, Indonesia, captured on 27 September 2005 by the MODIS (Moderate Resolution Imaging Spectroradiometer) instrument aboard NASA's Aqua satellite. The extent of such fires is likely to increase if climate warming causes the Asian monsoon to intensify.

MODIS/NASA/GSFC