Unfortunately, the noise in the final image also increases with microcrystal size[13]. So, higher and higher film speeds can be reached, but the image tends towards lower quality, particularly when enlargements are made. Increasing the efficiency of latent-image formation is a much better, although more difficult, way to achieve higher film speed.

The work of Belloni *et al.*[4] shows one way to do this without incurring problems related to reduction sensitization. The use of formate (HCO_2^-) as a dopant is a novel way to overcome the residual recombination in conventionally sensitized microcrystals. Not only does it appear to be efficient at destroying holes, but the resulting unstable CO_2^- radical is able to provide an extra electron for latent-image formation. Now the theoretical limit becomes two silver atoms per photon. Similar results have been observed with reduction sensitization, but never without some risk of fogging[10,11,14,15].

Silver bromide emulsions, such as the one studied by Belloni *et al.*, only absorb blue light. This is because quantum theory dictates that discrete (rather than continuous) energy levels are formed in the crystal lattice, creating a permitted 'conduction band' for free electrons with the right energy. To capture and display the full colour of the original scene it is necessary to use spectral sensitization in addition to chemical sensitization. In spectral sensitization, dyes are adsorbed on the microcrystal surface and provide absorption in the region of the spectrum where the microcrystal is unable to respond[16]. The absorption event places an electron in a higher energy state, from where it can be transferred to the conduction band of the microcrystal and then participate in the usual process of latent-image formation (Fig. 1). Unfortunately the dye also introduces an energy level for trapping holes, making it more difficult for the formate ions to destroy them.

If formate doping is to be effective in increasing the sensitivity of dyed microcrystals it is necessary for the photogenerated hole to transfer to the valence band of the silver bromide crystal. Otherwise holes trapped by the dye act as recombination centres. Belloni *et al.* show that the hole will move into the valence band for a dye absorbing in the mid-green region, although the sensitivity increase is less than what they see with undyed microcrystals. One might suspect that this lower degree of efficiency is due to hole trapping by the dye so that holes are less likely to be destroyed by the formate dopant. Furthermore, one might expect the degree of sensitivity improvement to be even less for dyes absorbing in the red region, where holes are even more deeply trapped (Fig. 1). Studies with red dyes will be important for assessing the general value of formate doping as a way to remove residual inefficiencies in the photographic process and achieve the highest sensitivity possible.■

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Neural networks

Evolutionary checkers

Igor Aleksander

It was headline news in May of 1997 when the IBM computer 'Big Blue' beat chess champion Gary Kasparov. So why is it that Kumar Chellapilla of the University of California in San Diego and David Fogel of Natural Selection Inc. have written two papers[1,2] in which they suggest that this seeming triumph "is testament to the limitation" of the very idea of artificial intelligence?

Artificial intelligence is often hailed as a new development, but the year 2000 will see its fiftieth birthday. In 1950 Bell Laboratories engineer Claude Shannon wrote the first chess-playing program for a computer. This allowed computers to hatch out of the shell of numerical calculations and perform tasks that could be said to require logical 'thought'. Shannon showed[3] that the game of chess could be reduced to numerical manipulation through the invention of a 'minimax' algorithm that allowed a computer to choose a good move without having to evaluate all the states in the intervening moves. This became proof that the number-crunching abilities of computers could be used to perform tasks which, if done by humans, would be said to require intelligence.

Chellapilla and Fogel's critique is based

Ergonomics

Suffering for one's science

Was Alexander Fleming a martyr to backache? If this picture is anything to go by, he probably was — along with 80% of long-term microscope users. They are also afflicted with eye strain, a variety of muscular pains and tension headache. Help is at hand, though, from Alfons Kreczy and his colleagues (*Lancet* **354,** 1701–1702; 1999).

Kreczy *et al.* designed a workstation to straighten out the hunched posture of microscopists. They adapted the eyepieces so that they could be used with only a 5° downward tilt of the head. They built an elevated table for the microscope with supports for the forearms. And they installed a chair that encouraged an upright sitting position and supported the lower back.

DAILY HERALD ARCHIVE/NMPFT

They then compared the muscle activity of users of the new, improved workstation with that of people sitting in an ordinary chair and using an ordinary microscope perched on a pile of books. The ergonomic workstation resulted in a big decrease in the activity of the most strained muscle groups — those of the neck, arms and lower back. Unfortunately, eye strain is an unavoidable consequence of scanning lots of slides.

Maintaining an unhealthy posture over a long period results in pain starting more quickly and taking longer to go away. Eventually it will carry over into rest periods and even, research on postal workers has found, into retirement.

So if you find yourself getting up from your microscope, clapping one hand to your forehead, the other to your back, and emitting a heartfelt groan, you might want to show this copy of *The Lancet* to your boss. **John Whitfield**

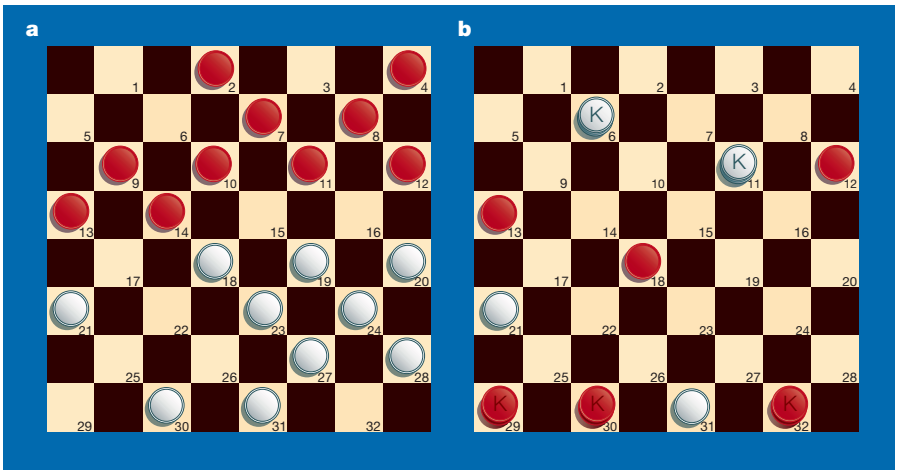

Figure 1 **A checker-playing neural network from generation 230 of Chellapilla and Fogel's evolutionary series takes on a human player, and wins.** a, **A turning point in the game comes at move number 11 when white (the human) walks into a trap set by red (the neural network). Red moves 11→16; white is then forced to move 20→11, whereupon red strikes: 8→15→22. White is one down and never recovers.** b, **The endgame. It is move 32 and white is now down by a piece and a king (K). Red has just moved 14→18, and white's pieces on 21 and 31 are pinned down . With an endgame of three kings (red) versus two kings (white) in sight, white resigns. (Redrawn from ref. 1.)**

on an approach that avoids the need for a programmer to work out the game-playing program. It uses evolution in artificial neural networks which, they argue, is an advance both for artificial intelligence and the design of such networks. The proposed artificial evolution encourages the survival of those systems in a batch that exhibit success in beating artificial opponents. New batches are derived from successful networks and the process is repeated until some good playing strategies have evolved. Such strategies have been shown to beat human experts. The game in Chellapilla and Fogel's case is not chess but checkers, or draughts as it is called in Britain. The authors point forcefully to the fact that the evolutionary process actually creates its own intelligence rather than relying on that of a programmer. Referring to the method that eventually defeated Kasparov, they write: "Every 'item' of knowledge was pre-programmed. In some cases the programs were even tuned to defeat particular opponents ...".

Although neural networks were first suggested in the early 1940s, it is only in the past 15 years or so that they have been used with some success as systems that can learn to recognize patterns in a variety of scientific and industrial applications. Conventionally they consist of layers of cells (artificial neurons) where interconnections between neurons in adjoining layers are made through 'weights', while the body of the cell performs summations that cause it to 'fire' at an output (the axon) when the incoming weighted activity overcomes some mathematically specified gradient function. The weights are thought to resemble the action of synapses in real neuronal cells found in biological brains, where neurons connect and learning takes place through the alteration of such weights.

So an artificial network (which can have one of many popular topologies) learns to approximate an input–output function by being given examples of the in- and out-values of such a function. It does this through one of a variety of weight-adjustment procedures known as learning algorithms. The learned tasks can be as esoteric as recognizing faces where it would be hard for a programmer to work out *a priori* a function that would distinguish between such patterns. However the techniques used by Chellapilla and Fogel do not make use of learning algorithms such as these, but arrive at suitable synaptic-weight functions through an evolutionary process.

They use a population of 15 neural networks with randomly selected weights and the 'offspring' of such parent networks containing a variation of the parents' weights. The task for the network is to evaluate board images, while the playing proceeds along Shannon's minimax lines. All parents and offspring play five games against opponents randomly selected from their midst and are awarded points based on their successes and failures. The 15 most successful networks are then chosen to be the new generation, offspring are produced and the process repeats. One hundred generations take about two days of computing on a 400 MHz Pentium machine. After 250 generations the best network is chosen to play human all-comers on the Internet, who in turn are evaluated in terms of the excellence of their playing on a national categorization. The network was able to achieve a top categorization (that is, 'A') on this scale, to defeat two 'expert' category players and to draw with a 'master'.

Chellapilla and Fogel stress that evolutionary methods can develop machine intelligence without being programmed, and

100 YEARS AGO

During two or three visits to Paris and Nice some years ago, I discussed with many French astronomers, whom I was privileged to count among my personal friends, the question of the large telescopes of the future. Among the conclusions come to, the first was that the glass industry was not in a position to grapple with astronomical requirements, and hence when reflectors of 8 or 10 feet diameter were talked of it was understood that they must be made of porcelain with a glass surface. … During the last few years we have heard a great deal of an enormous telescope to be constructed on the occasion of the Paris Exhibition of 1900; a reflector of 10 feet aperture, such as was discussed in 1875, but it would seem that now as then the glass industry is not able to furnish a disc of this size, for after all it has been determined to construct a refractor, and mount it as I suggested nearly twenty years ago in front of a siderostat. … It is the intention of the Syndicate to erect in connection with this telescope a Palais de l'Optique near the Eiffel Tower, containing a hall capable of holding some 4000 persons, and in fine weather images of the various celestial bodies are to be thrown on a screen 20 metres in the side by means of secondary magnifiers. Thus an image of the moon 16 metres in diameter, and of Mars 3.70 metres in diameter, are promised to the abonnés.
From *Nature* 21 December 1899.

50 YEARS AGO

Only two large mammals of South Africa have become extinct in the historical period, namely, the quagga and the blue buck. The blue buck (*Hippotragus leucophoeus*) lived in the south-west part of Cape Colony, and is believed to have been exterminated about 1799. About half a dozen mounted specimens have been preserved, mostly rather bad, and perhaps about three more pairs of horns exist the determination of which is doubtful. No specimen of the skull is known to exist, except, perhaps in some of the mounted specimens. On recently visiting the Hunterian Museum (Zoological Section) at the University of Glasgow, I saw a specimen that at once struck me as probably the skull of the extinct blue buck. There is no history attached to the specimen; but it is believed to have belonged to the Hunterian Collection. As William Hunter died in 1783, the specimen could date back to about the middle of the eighteenth century.
From *Nature* 24 December 1949.

demonstrate[1] some of the generality of this principle in other games such as tic-tac-toe (noughts and crosses) and those involving a mix of collaborative strategies between the players (the so-called Prisoner's Dilemma). All of this shows that organisms in nature achieve what is called intelligence through a fascinating mix of evolution, adaptation and learning — with the possibility of inspiring those interested in computation not only to build smarter machines but also to get a better understanding of the nature of intelligence itself. ■

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Diabetes

Insulin resistance and obesity

Michael W. Schwartz and Steven E. Kahn

Type 2 diabetes mellitus is a serious health problem in the Western world. It arises when resistance to the glucose-lowering effects of insulin combines with impaired insulin secretion to raise the levels of glucose in the blood beyond the normal range. Studies into the molecular basis of insulin resistance have focused on the peroxisome proliferator-activated receptor gamma (PPARγ). This molecule, a member of the nuclear-hormone-receptor family, is the cellular target of thiazolidinedione drugs, which are used to treat diabetes by increasing sensitivity to insulin.

What are the endogenous ligands for PPARγ? How does it promote the insulin-stimulated uptake of glucose? And is this effect essential for the normal action of insulin? The answer to the last of these questions may be nearer thanks to a study by Barroso *et al.*[1] on page 880 of this issue. They report the identification of two loss-of-function mutations of PPARγ that are associated with severe insulin resistance and type 2 diabetes mellitus in humans. Although such mutations are rare — detected in just three of 85 insulin-resistant people, and none of 314 controls — the implication that PPARγ is required for normal insulin sensitivity in humans is an important advance.

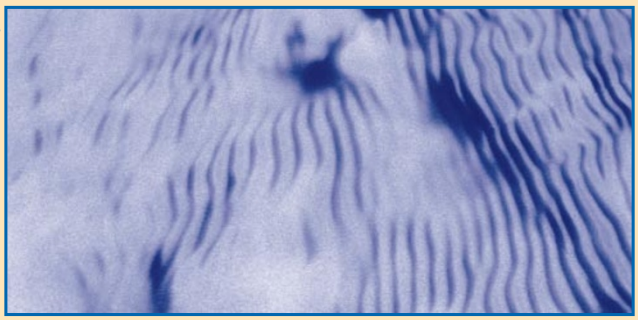
Found in the nucleus of many cells, particularly fat cells, PPARγ is both a receptor and a transcription factor. When PPARγ is bound by ligand, such as a thiazolidinedione, it becomes activated and binds to specific DNA sequences in gene promoters. Then, in complex with another transcription factor known as the retinoid X receptor (RXR), it activates the transcription of specific genes[2] (Fig. 1, overleaf). One of the best-studied effects of activated PPARγ is its ability to induce differentiation of fibroblasts or other undifferentiated cells into mature fat cells[2]. Signalling by the PPARγ–RXR complex is also implicated in the synthesis of biologically active compounds by vascular endothelial cells[3] and circulating immune cells[4]. Mutations in PPARγ may contribute to cancer[5], and increased PPARγ signalling (owing to a mutation that increases its intrinsic activity) is also associated with human obesity[6].

Barroso *et al.*[1] now show that the people affected by loss-of-function PPARγ mutations (one affects a mother and her son; the other affects an unrelated woman) share common elements of the 'insulin resistance syndrome'. Symptoms include insulin resistance, diabetes, high blood pressure, dyslipidaemia (an abnormal plasma-lipid profile) and a skin-pigmentation disorder known as acanthosis nigricans. But a cardinal feature of the insulin-resistance syndrome that these people do not show is obesity. Reduced PPARγ signalling therefore seems to cause insulin resistance in the absence of obesity.

This observation contrasts sharply with the symptoms of gain-of-function mutation of PPARγ, reported last year by Ristow *et al.*[6]. In their study, obesity was associated with relatively low levels of insulin, suggesting an *increased* sensitivity to insulin. However, neither report[1,6] includes a measurement of insulin sensitivity. Moreover, a third mutation in PPARγ has variable effects on body weight and insulin sensitivity[2,7,8]. Nevertheless, all of these findings indicate that by increasing PPARγ function it may be possible to prevent insulin resistance from occurring when normally it would (for example, in the obese state). Conversely, mutations in PPARγ that cause reduced function could lead to insulin resistance in lean people, in whom it would not normally occur.

Antarctica

Vast snow dunes frozen in time



NASA GODDARD SPACE FLIGHT CENTER

Release of data gathered during the Cold War continues to deliver scientific surprises. The latest example emerged at last week's American Geophysical Union meeting in San Francisco, where glaciologists reported new findings about Antarctica based on satellite data. The revelation came from comparisons of modern satellite images of snow dunes (such as the one shown here) with recently declassified pictures originally taken by intelligence satellites in 1963.

The first complete map of Antarctica, produced in 1997 with data from the Canadian satellite Radarsat, revealed many unexpected features, including vast tracts of snow dunes. These megadunes are up to 100 kilometres long, lie 1 or 2 kilometres apart but are only a few metres high. In East Antarctica fields of the dunes cover an area larger than the state of California.

At the meeting Mark Fahnestock (University of Maryland) described how he and Ted Scambos (University of Colorado) compared data from satellites of the US National Oceanic and Atmospheric Administration and from the 1960s military images. It might be thought that the snow dunes would move, even if only slowly, because of the fierce, constant winds that blow across the East Antarctic plateau. It turns out, however, that they have not — at least over the past 30 years. Little is known about how the megadunes formed, but it is unlikely that they grew from drifting snow in the way that sand dunes are built from sand.

Across the other side of the continent, on the West Antarctic ice sheet, vast streams of ice flow into the sea. The source of the ice streams has so far eluded explorers and satellites alike. At another talk at the meeting, Robert Bindschadler (NASA Goddard Space Flight Center) described high-resolution data from Radarsat that reveals several small and slow-flowing tributaries that are feeding the large frozen rivers with snow from the interior. One of the biggest uncertainties in predicting sea-level rises in response to climate change is the uncertain behaviour of the Antarctic ice sheets. So new data (however old) is always welcome. **Sarah Tomlin**