

Although such networks appear more accurate than traditional statistical methods,^{6,7} their inner workings are hidden within a black box. The black box has hindered widespread acceptance of artificial neural networks, because it prevents validation and network interrogation. This lack of acceptance and hidden inner workings might be overcome with an alternative form of artificial intelligence based on fuzzy logic.⁷

Wei and colleagues⁴ studied 49 patients with neuroblastoma, the most common solid extracranial malignancy in childhood. To guide their treatment, patients were conventionally stratified into high, intermediate, and low risk, by several factors, including age at diagnosis, histological features, tumour stage, and amplification of the *MYCN* oncogene.⁸ As with most clinical classifications, this system is imperfect. About 30% of high-risk patients have prolonged survival, and 15% of low-risk patients progress despite treatment.^{4,8} Wei tried to improve the accuracy of this stratification by using artificial neural networks to model gene-array data. Having analysed 25 000 genes in each sample, the researchers used networks to identify the most relevant predictive genes. By repeating the model while varying the input for each individual gene, the researchers identified the genes that most altered the predictive accuracy of the model (19 genes). This selection was successfully validated in their analysis. A new model trained with these 19 genes more accurately predicted survival than both a previous model with 25 000 genes and the current clinical classification. Furthermore, when only high-risk patients (according to conventional criteria) were analysed, a 19-gene network was able to identify the small proportion of patients that would respond to treatment. It is the remarkable ease with which this approach identifies and validates important genes that highlights its very benefit. Of the 19 genes identified, seven are unknown (so-called expressed sequence tags; RNA sequences produced by cells whose gene identity is yet to be established), and two genes are currently used for neuroblastoma prediction; *MYCN* and *CD44*. Wei and colleagues were therefore able to identify ten new prognostic genes, seven of which are expressed in neural tissue. However, no single marker alone was able to accurately classify patients.

Although the scientific community anticipated that single molecular markers, such as TP53, could have sufficient

power to accurately classify tumours according to behaviour and response to treatment, this approach is now recognised as unrealistic because of the complexity and interdependence of molecular mechanisms leading to the behaviour of diseases. The future of molecular diagnostics and prognostics undoubtedly lies in validation of panels of selected markers, which will complement conventional pathological classifications. Wei and colleagues⁴ elegantly showed that as few as 19 genes can predict outcomes for neuroblastoma, and other reports have produced similar results in other cancers.⁹ These novel experimental and analytical approaches are invaluable, and they require urgent attention and investment. It is likely they will pave the way to translate molecular knowledge from the bench to the bedside, a much awaited result of the concerted efforts of scientists and clinicians in years to come—an outcome that will benefit our patients.

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Climate change, health, and development goals

Recently, a consortium of development and environmental non-governmental organisations published *Up in Smoke*.¹ This report acknowledges the fundamental interdependence of development and the environment. It recognises that humanity already faces protracted, mostly hazardous, environmental and social consequences of climate change—despite whatever immediate action we might take to mitigate emissions of greenhouse gases.

Up in Smoke explores the effects of climate change on key development processes in poor countries: freshwater supplies, agricultural yields, physical safety, human settlements and infrastructure, health, and economic and gender equity. Overall, the omens are not good. Climate change will amplify existing hazards, deficits, and inequities, jeopardising the already low status of population health and well-being of disadvantaged populations. This bleak outlook

echoes a conclusion of the UN's Intergovernmental Panel on Climate Change: "The impacts of climate change will fall disproportionately upon developing countries and the poor . . . exacerbating inequities in health status and access to adequate food, clean water and other resources."²

It is important to identify those populations most at risk of adverse effects from climate change, to reduce their vulnerability. An analysis of the world's geophysical systems identified tipping points where the effects of climate change would be critical—such as step-changes in the Gulf Stream circulation, the Asian Monsoon, the Sahara Desert, and the Antarctic ice-sheets.³ By contrast, there has been no systematic attempt to identify the most vulnerable human communities and the main health risks they face.

By emphasising the links between adverse environmental change and poverty, *Up In Smoke* provides a springboard to strengthen the next formulation of the Millennium Development Goals. Four of the eight goals⁴ refer to health: eradicating extreme poverty and hunger; reducing child mortality; improving maternal health; and combating HIV/AIDS, malaria, and other diseases. Only one refers to environmental sustainability and thus bears on global climate change. But without environmental sustainability the other Millennium Development Goals are extremely fragile. For example, the Maldives might achieve universal access to sanitation and safe water by 2015, yet become uninhabitable within two centuries because of rising sea levels caused by climate change. Many policy-makers seem not yet to understand that sustainability is not merely an embellishment of our targets; it is about maintaining critical stocks of natural resources and the functioning of the biogeophysical systems on which life depends.

If giving preference to long-term environmental sustainability were to lead to immediate needs being ignored, then the other Millennium Development Goals might be jeopardised. But they need not, because another critical element connects health, poverty, and environmental sustainability: namely, human population growth. Humanity's increasing ecological footprint⁵ reflects both increasing per-capita consumption and increasing population. At the risk of sounding old-fashioned, we believe that (sustainable) development offers the best chance of reducing population growth, other than via disease, conflict, or coercion. Advancing the seven Millennium Development Goals that are related to development (which include universal primary education and sex equality) will slow rates of population growth, thereby enhancing development⁶ and reducing the final size of the ecological footprint.

Cooperation between the development community and the green movement has probably been inhibited by suspicion that focusing on environmental sustainability could be used to justify continuing low environmental-impact poverty. Similarly, releasing the family-planning genie from its currently well stoppered bottle may revive fears

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over minority rights, forced sterilisation, and rich-world paternalism. Slower population growth might also expose covert economic anxieties, including concern about a reduced supply of cheap labour (that could support ageing populations in rich countries). Those working in development, rights, justice, and sustainability must address these fears. Reducing the magnitude of the future peak in the global population need not entail injustice. Indeed a smaller maximum population would probably be a consequence of a world that is fairer than at present. Although this approach cannot itself prevent some degree of global climate change, it will at least create some chance of coping with its effects.

Up in Smoke underscores the crucial links by which climate change jeopardises development. As noted: "By divorcing the global warming debate from the development debate, half of this disaster equation is ignored. Worse still, conventional economic development is undermining the markets and safety nets of developing countries and reducing their capacities to cope with climate change."⁷ This complex multidirectional relation needs urgent research and policy attention.

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CDB has received travel expenses from the Millennium Ecosystem Assessment and WHO to discuss issues related to environmental change and health. I am also co-founder of an NGO called BODHI (<http://www.bodhi.net.au>). AJM has no conflict of interest.

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Women are catching up, fast—perhaps

So, if female athletic performance keeps improving at the present rate, the Olympic 100 m track—by then presumably a unisex gathering-place, like many hair salons, hospital wards, and toilets today—will be dominated by women in 2156. The winner will have reached a speed that would get today's motorists into trouble in a built-up area. I suppose that if this linearity has no end, by some far-off Olympiad she will be hitting the finishing tape side by side with the sound of the starting pistol. Andrew Tatem and colleagues have found that there is nothing fancy about the relations between winning times and the year the race was held; for men and for women winning times have improved in almost straight lines so far, with the women making the more rapid improvement.¹ This simple linearity is rather surprising, especially because, on the eve of this year's Olympics in Greece, a well-researched news report in *Science* was sceptical about the closure of this gap between the sexes.²

In chapter 17 of *Life on the Mississippi* Mark Twain noted the river's habit of taking occasional short-cuts and he mischievously estimated that at the prevailing shrinkage rate it would be down to only about 3 km seven centuries on. "One gets such wholesale returns of conjecture out of such trifling investment of fact", he noted. The river runs yet, no doubt chortling to itself *reductio ad absurdum*. Whether Tatem and colleagues' far-reaching prediction will prove absurd is for future generations to discover, unless something even more surprising is happening to life expectancy.

In the very ancient games, married women were not allowed even to watch. We have come a long way since then, but slowly. In 1900, the chaotic Olympics year when a runners-up medal for cricket could be won by expatriate Britons playing as "France", even though there were only two entrants, there was no room for women in the major events. The founder of the Olympic revival, Baron Pierre de Coubertin, saw no place for female competitors, in public at least, and women competed in track events for the first time in 1928.³ Any current rapid improvement in female performance could be explained, at least in part, by increased participation in sport generally. Between 1900 and 2000 the sex ratio of participants in the Olympics dropped from 80:1 to 1.6:1.⁴ The relative gaps between the winning times of the men's and women's 100 m races since the con-

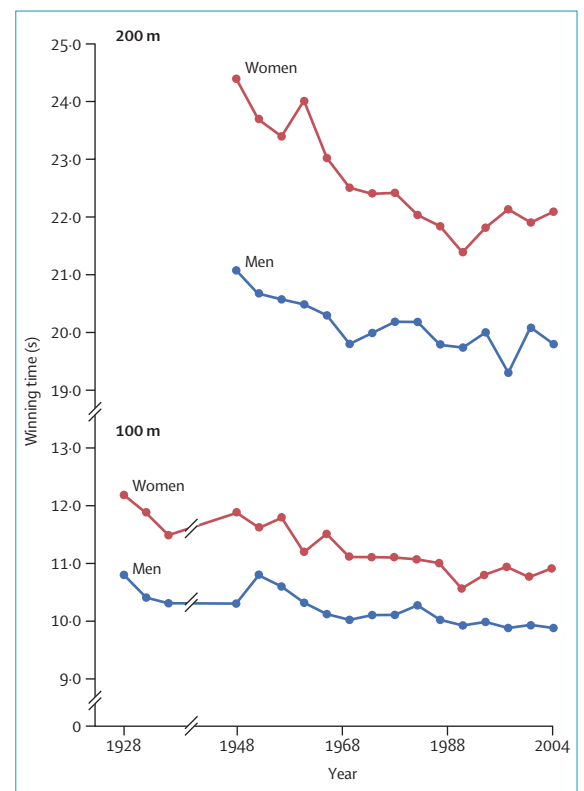


Figure: Times for 100 m and 200 m Olympic gold medalists

troversial Moscow games of 1980⁵ (figure), do not improve my confidence in predicting what might happen in Beijing.

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