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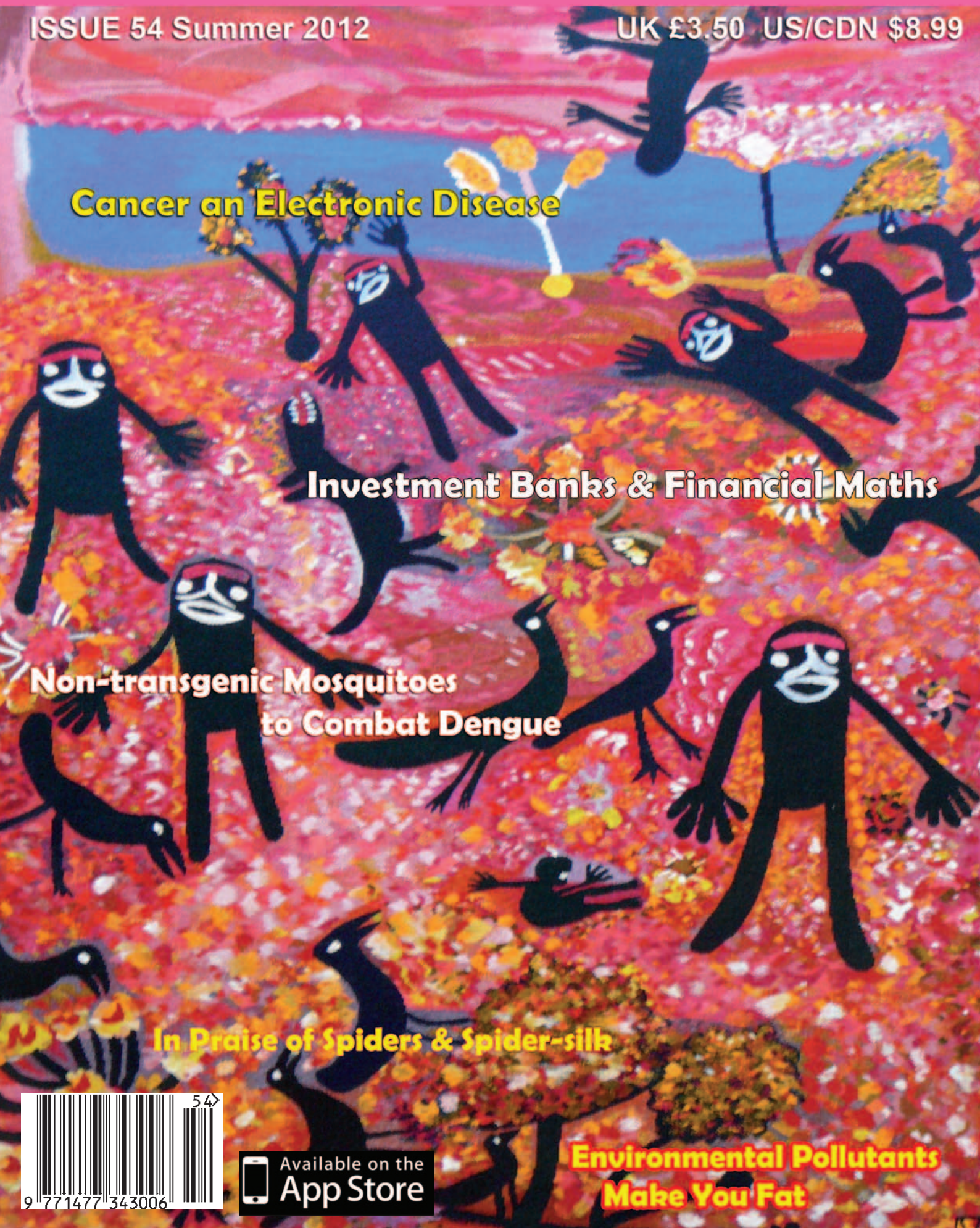

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Investment Banks & Financial Maths

Time to call the bankers' bluff

As the result of the credit crunch, most workers in the UK are watching their real incomes fall and their pension rights eroded. Those out of work have little prospect of finding a job in the foreseeable future. There is a big squeeze in expenditure on education, health, welfare, and almost every essential service we have come to expect the state to provide. Worst of all, young people finishing their education are finding it very hard to get started in the jobs market. In the three months to December 2011, unemployment among 16-24 year olds was 22.2 %. By the end of the first quarter in 2012, UK is back in recession. Meanwhile, the bankers largely responsible for what has happened, and who would be out of business if the taxpayers hadn't handed over £90 billion to bail them out continue to draw huge salaries with bonuses on top.

Why should those who are the most responsible for the financial disaster continue to see their standard of living rise year by year when the rest of us get poorer and poorer?

The answer is simple if unedifying, so we are told. Ever since the deregulation "Big Bang" of 1986, the UK economy has become more and more dependent on financial services. Successive governments have talked about promoting industry but it has been the City that got what it wanted, including the "light touch" regulation that encouraged the bubble to expand so dangerously. That doesn't seem as good an idea today as it did at the time, but the hard fact is that now we have to give the investment bankers everything they want or they'll pack their bags and go, taking what remains of our economy with them.

Or will they? According to the financial pages of the London papers at the end of February 2012, the UK division of the international recruiting agency Hays lost £3 million in 2011. A major reason was the recruitment squeeze in banking, not just in the UK but around the world. Hays' chief executive Alistair Cox told the press: "A year ago we said that a lot of bankers were looking for jobs out in Asia. We still see that, but the banking sector has slowed down globally. Banking started to get worse four to five months ago. I don't think it will get any better soon." He added, "It's quite uniform worldwide, not just focused on the UK. We see the impact in Hong Kong and Singapore and particularly in investment banking, as opposed to retail banking."

That is good news for the vast majority of ordinary people that do not make their living gambling with other people's money as investment bankers do. We need a return to high street banks and cooperatives that serve local communities and the real economy of goods and services (see New Economy *Now*, *SiS* 53).

It is now clear that if those self-styled masters of the universe really do leave the City, they're not going to better jobs abroad because there aren't any. Their threats are bluffs, something we would expect people in investment banking to be good at.

While Hays' UK division lost money last year, the company as a whole made a profit of £60 million for the six months up to December 2011. That is because it earns 70 % of its fees outside the UK, and recruitment in professions such as engineering is holding up well in Germany, the US, the Middle East and East Asia, again, a sign that those countries are taking the real economy very seriously. It looks like it will be better to be making things rather than just pushing money around. And if sanity ever returns to the world of finance, the banks may well move to the Far East, not to avoid taxes and regulation but because that is where the centre of the world's economy will be.

In the end, that might not be such a bad thing for the UK, which has become too dependent on the financial services sector and not on the real economy. That made it especially vulnerable in the crash following the sub-prime mortgages collapse, and also to any threat by the banks to move.

Characteristically, the government's reaction to the credit crunch was to pour massive amounts of money into the banks. They apparently believed this would somehow trickle down into the real economy, but it has simply disappeared into the banks' coffers (see "Shut Down Wall Street!" *SiS* 53). With healthier balance sheets, the banks have felt able to continue to pay massive bonuses, but not to lend to the small and medium enterprises (SMEs) who need the money to build up the industrial strength that the government says it wants.

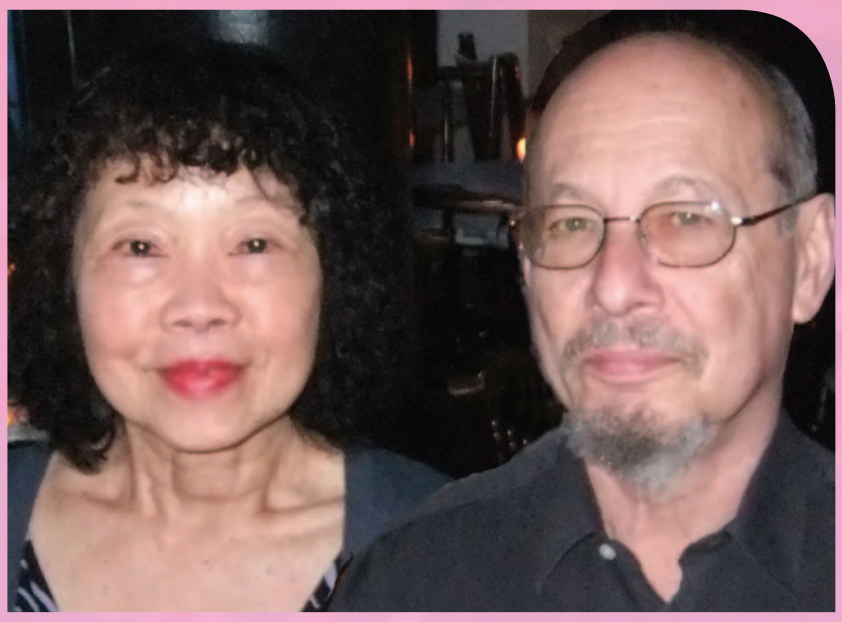
The UK needs to focus its attention on the real economy, a move that has already started to some extent in the US, at least at state and local levels.

Is financial maths to blame?

It is ironic that at a time when there is high unemployment especially among young people, industries are complaining of skill shortages. Too few young people are graduating as engineers and too many of those (almost half, according to the Institution of Mechanical Engineers) move into other careers. In contrast, there are far too many being trained to do 'financial' mathematics for devising and manipulating the complicated derivatives that were a major cause of the crash, and serious questions have been asked as to whether financial maths and mathematicians are to blame as much as investment bankers.

Are financial mathematicians responsible?

Incredibly, the 'blame' is limited to losing trillions. The debate focussed on whether the mathematical models



or data they used as input were good enough; the question of whether it is ethical to provide the mathematical instruments for creating credits out of repackaged debts and to gamble with people's live savings and livelihoods never entered into consideration. As one investment banker was quoted saying: "Banks need high level maths skills because that is how the bank makes money." Those deals that spiralled so badly out of control would not have been possible in the first place without the collusion of financial maths and financial mathematicians, known affectionately and awe-inspiringly as "quants" in the trade, commanding salaries typically in millions and above.

It is no use saying, as Professor William Perraudin, Chair of Finance at Imperial College London's Tanaka Business School did to the BBC: "The quants are a fairly innocent part of all this. It is the senior people who make decisions about taking on risk who bear the responsibility." Perraudin even went as far as to laud what the quants do as a great favour to society: "The quants have enabled financial institutions to behave in a super-efficient way, committing as little capital as possible to their activities." This has allowed relatively small competitors to take on the larger institutions in the provision of financial services and led, in turn to cheaper loans, he explained. Of course, that was also precisely responsible for the financial bubble.

Similarly, Chris Rogers, Professor of Statistical Science and head of the Quantitative Finance Group at the University of Cambridge, told a journalist: "The role of mathematicians in a bank is essentially a subordinate one, they are the servants of the business imperative."

Tim Johnson, Academic Fellow in Financial Mathematics based at Heriot-Watt University and the Maxwell Institute for Mathematical Sciences in Edinburgh, said in his own defence: "I was drawn into financial maths not because I was interested in finance, but because I was interested in making good decisions in the face of uncertainty...One of the key objectives of financial maths is to understand how to construct the best investment strategies that minimise risks in the real world." But he has not asked himself: minimise risks for whom and for what purpose that would serve humanity, or at least do them no harm.

However much the doyens of financial mathematics like to absolve themselves from blame, they bear major responsibility for providing the tools that enable one group of people (themselves included) to get prodigiously rich and beggar the rest of society.

It is time for aspiring mathematicians to wake up and consider their social responsibility and ideals as well as the beauty of mathematics. If financial bankers are losing their jobs, there certainly are not going to be many more jobs in financial mathematics either.

SiS

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Personalized Medicine for Cancer

Fact or Fiction?

Companies are marketing genetic profiling to provide personalized cancer therapy, but cancers show numerous mutations that differ not only between individual patients but also from one region to another in a single tumour

Dr. Mae-Wan Ho

Cancer as genetic disease dominate approach to therapy

For many years, cancer therapy concentrated on attacking DNA replication, as cancer cells proliferate and replicate their DNA rapidly. But these generally cytotoxic drugs also harmed cells that divide rapidly under normal circumstances such as bone marrow cells, cells in the digestive tract and hair follicles, with inevitable side-effects: decrease in blood cells and immune suppression, inflammation of the gut, and hair loss.

More recently, newer therapies target the abnormal biology of cancer cells based on the belief that cancer is a genetic disease involving mutations in key 'gatekeeper' cancer genes (oncogenes). These include signal transduction and protein turnover pathways, apoptosis (programmed cell suicide) and signalling receptors. Some of these agents exhibited antitumour activity and have been approved for cancer therapy, and new candidates are popping up all the time.

"the simple view of directing therapy on the basis of genetic tumour markers is probably too simplistic"

Still, there have been no cures in advanced cancers, though it is hoped that some combinations of agents may do the job.

Nevertheless, the field of cancer therapy has been gripped by an overoptimism that soon, patients with a tumour will undergo a needle biopsy, and a personalized treatment will be devised on the basis of the distinctive genetic characteristics of the tumour. Already, several companies are marketing tests for the genetic signature of a tumour, with the expectation that the genetic signature will determine the treatment and predict treatment outcome.

But a serious flaw in that imagined future of cancer therapy based on personalized medicine is the underestimation of tumour genetic heterogeneity; not just between tumours, but heterogeneity *within* an individual tumour. This was highlighted in an Editorial in the 8 March 2012 issue of the *New England Journal of Medicine*.

Profuse genetic heterogeneity between tumours and within tumours

In the same issue of the journal, a team of 30 researchers led by Marco Gerlinger from the Cancer Research UK London Research Institute mapped out in detail how heterogeneous a single tumour can be. Tumour samples were obtained from four patients with renal-cell cancer before and after treatment, with multiple samples taken from each patient's primary and metastatic tumour sites. The team carried out exome sequencing (sequencing of all regions that code for proteins, roughly 1 % of the entire human genome), chromosome aberration analysis and ploidy profiling (to determine how many sets of chromosomes are present instead of the usual two). They also characterized the consequences of genetic heterogeneity within a single tumour using immunohistochemical analysis, mutation functional analysis and profile of messenger RNA expression.

Over a hundred mutations are typically found in each patient (just in the coding regions of the genome; over the entire genome it would typically be thousands), and a branching phylogenetic (evolutionary) tree can be drawn based on shared mutations in different regions. About two thirds of the mutations found in single biopsies were not uniformly detectable throughout all the sampled regions of the same patient's tumour. Different regions of the same tumour gave a "favourable prognosis" and an "unfavourable prognosis" gene profile. There is no way a single tumour biopsy – the standard of tumour diagnosis and the cornerstone of personalized-medicine – can be considered to represent the genetic profile of the tumour, much less so, the cancer patient.

To make things worse, there are widespread alterations in the total number of chromosomes in the tumour cells (aneuploidy), and many allelic imbalances are found in which one allele of a gene pair is lost, either due to chromosome loss, or difference in gene imprinting that alter gene expression.

Another finding is that different regions of the tumour have different mutations in the very same genes (convergent evolution), suggesting that parallel alterations in epigenetic mechanisms (not immediately involving gene mutations) and signal transduction have taken place to ensure the tumour's survival.

All that is part and parcel of the fluid genome of cells responding to their microenvironment within the body (see Living with the Fluid Genome, ISIS publication). But most cancer researchers have not faced up to the possibility that most, if not all the genetic mutations and genomic instability are effects, rather than causes of cancer (see later).

We shall look at cancer prevention and cure in depth in this special series of articles.

Personalized medicine in jeopardy?

Clearly, the lab findings create practical problems for personalised medicine in cancer therapy, as pointed out by both the commentator and researchers. Sampling bias in biopsies could fail to identify key cancer markers and contribute to selection of drug resistant clones, or else fail to predict drug resistance to therapy.

Despite that, neither the Editorial nor the researchers give up hope on personalized medicine. The identification of common mutations in the trunk of the tumour's phylogenetic tree confirm that the genetic lesions in the original tumour cells are consistently expressed, such as the von Hippel-Lindau gene in renal-cell cancer, and may be a more robust target for therapy. In addition, the genes affected by convergent evolution may be suitable targets for functional inhibition or restoration.

"However", the Editorial concludes, "the simple view of directing therapy on the basis of genetic tumour markers is

Tic Tac Toe *by Kathy Haffegee, UK*

probably too simplistic."

Cancer is not a genetic disease

There is, of course, the possibility that the genetic approach is misplaced. The gene mutations, even those in common 'gate-keeper' genes could be effects of a more fundamental cause. This is entirely likely given the fluidity of the genome, the ease with which genes can be silenced or activated, and both RNA and DNA sequence changes can occur in response to the environment as described in detail in my book. It would also be consistent with the evidence that the causes of cancers are overwhelmingly environmental. An increase in somatic mutation rate provoked as the result of a stress response, for example, could explain why numerous different mutational changes are typically found from one individual cancer patient to the next, and even within a single tumour. Personalized medicine in cancer therapy may well be extremely time-consuming and costly, if not downright misdirected. Cancer cells under attack in one pathway can switch to another pathway, or else develop drug resistance that enable them to survive and multiply, as bitter experience in cancer therapy has revealed.

There is evidence in support of the view that cells become cancerous as the result of epigenetic 'adaptive' mutations in response to chronic stress or environmental stimuli that promote cell proliferation (Cancer an Epigenetic Disease, *SiS* 54).

Furthermore, by far the most general manifestation of cancer is an abnormality in energy metabolism (Cancer a Redox Disease, *SiS* 54), which may lend itself to affordable and safer therapies for all (see Does DCA Cure Cancer? *SiS* 54).

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