

Comment

## When bubbles burst

Gregory A Petsko

Address: Rosenstiel Basic Medical Sciences Research Center, Brandeis University, Waltham, MA 02454-9110, USA.  
Email: [petsko@brandeis.edu](mailto:petsko@brandeis.edu)

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Chutzpah used to be defined as audacity so shameless that the usual example was someone who murdered his parents and then asked for mercy because he was an orphan. These days, an even better example would be that of the chief executives of financial firms, a group of - typically, but not always - conservative Republicans who, having spent much of the past decade railing about the evils of big government and trumpeting the virtues of the free market, are now traipsing in droves to Washington, whining to that same big government to save them from - you guessed it - the free market. If you or I were to do the same when we lost money at the racetrack, Washington would have a good laugh at our expense. So these captains of industry got the same response to their naked hypocrisy, right?

Yeah, right. At the time of writing, the US government has spent, by some accounts, approximately \$900 billion over the last year or so to prop up the failing financial services and mortgage industries. Now the Bush Administration is asking Congress for authority to borrow another \$700 billion to buy up mortgage-backed securities, to prevent the financial sector from collapsing altogether. Congress is still wrangling over the details, but it seems almost certain that some sort of bailout will have been passed by the time you read this. Let's forget about the money they've already spent and consider just that \$700 billion sum. That would fund the National Institutes of Health for the next 25 years, and is more than twice as much as the government has spent on all biomedical research in the past 100 years. No wonder nobody can get a grant.

(Come to think of it, maybe we've been going about this the wrong way. Instead of applying for more grants, maybe each of us should just overspend our existing grants by, say, several million dollars, and then the scientific community could demand that Congress bail out the NIH rather than let the biomedical establishment go bust. Just a thought.)

What's caused all this, of course, is the bursting of an asset price bubble. One of the meanings of the word 'bubble' is a

state of expansion that is unstable and so is unlikely to last. Remember the 'dotcom' bubble of the 1990s, so named because employees of companies doing business on the internet were making huge paper profits from options to buy stock in their overvalued companies, and millions of investors were driving the prices of those stocks ever higher in a frenzied attempt to get rich too. When people realized that almost none of these companies could ever make a profit, the bubble burst and internet company stock fell faster than a 3-tonne safe dropped off the Eiffel Tower. Companies with no products and no income, yet whose paper value had once exceeded that of the Ford Motor Company, became worthless - which was, of course, their true worth - overnight. It took the spectacular successes of Amazon, eBay and Google to restore some investor confidence in internet businesses.

The real-estate bubble that occurred in Japan in the 1980s is even more instructive because of its disturbing parallels with the present situation. Then, prices of commercial properties in Tokyo and other Japanese cities skyrocketed to the point where some offices - not office buildings, just offices - were among the priciest real estate on Earth. The fact that their intrinsic value was obviously much less didn't stop companies from buying them as investments and - here's the real parallel - didn't stop banks from both lending huge sums of money to buy them (after all, their value would go up forever, right?) and, worse still, using them as collateral to cover their own borrowing. When the value of that property began to fall, the entire financial sector was so entangled that the bursting bubble triggered an economic depression in Japan from which that country has still not completely recovered.

In much the same way, the current worldwide financial crisis, considered by some commentators as the most serious since 1929, was triggered by overvalued real estate - in this case, homes. Without going into a lecture on finance - which I'm not remotely qualified to give - let's just say that the

United States is now paying the price for living beyond its means for the past ten years. Foreign investors, eager for the high returns and stability that Wall Street represented, poured money into the financial markets here. But for the most part, the investment banks and brokerage firms that took in that money didn't invest their profits in infrastructure improvements or job-creating new industries. Instead, they put the money into risky home mortgages and then went after even bigger profits by creating a dizzying array of complex financial instruments (such as derivatives and hedge funds), most of which were based on borrowed money secured by those same mortgages. Housing prices were going to go up for ever, weren't they? People were always going to need a place to live, right? And individuals also borrowed vast sums of money to fund a spending spree, secure in the knowledge that they had the wealth to cover their debt in the form of their suddenly valuable homes.

Inevitably, the overvaluation of houses created one of the great bubbles of our time, and when it burst, it did so spectacularly. As house prices fell and people defaulted on their mortgage payments in the shrinking economy, the assets that secured the vast, borrowing-driven boom in the financial sector became insufficient to cover all that debt. The past few months have seen one financial giant after another go bankrupt, or be taken over by the government, or be bought for pennies on the dollar.

But what, you are certainly asking by now, has all this got to do with genome biology? If a bubble occurs when things assume a value way out of proportion to their true worth, then big science, which in biology is epitomized by genomics, may be on its way to becoming one. As I've pointed out before, the success of the Human Genome Project, not only from a scientific perspective but also in terms of commanding both resources and attention, spawned a host of imitators. Some of the resulting large-scale, technology-driven, data-gathering projects have real value. Others, like the Structural Genomics Initiative and the Cancer Genome Project, have, in my opinion, much less. Yet the failure to terminate the former or to realize that the data gathered by the latter may not be very useful (owing to, among other things, the heterogeneity within any one tumor), argue that these 'assets' have a perceived value way above what they should have.

Value to whom? Well, certainly to the people being funded by them, but also, I think, to the scientific administrators in Washington who can use them to point to the productivity of the institutes and programs they manage. We might be able to live with that if it weren't for one thing: the pie is finite. Two plus two makes four, not five or six, and when someone takes two out of four there is only two left. A lot of these projects have earmarked funding; they do not compete in open peer review against your grants and mine. They are evaluated on their own by *ad hoc* reviewing panels, and even

when those evaluations are scathing, as was the recent evaluation of the Structural Genomics Initiative, they rarely lead to the program's termination. A severely negative review of an individual's research proposal typically results in that grant never being funded or not being renewed. Big-science projects typically just have their objectives repackaged.

The enormous paper wealth created by the financial bubble didn't enrich anyone but the financial industry itself. While brokers, traders and chief executives raked in bloated salaries and obscene bonuses, the infrastructure of the United States crumbled, job creation almost stopped, the social fabric rotted, and the federal budget surplus bequeathed to the Bush Administration by the Clinton Administration shrank into a deficit that is now the biggest in the country's history. Similarly, I worry that many of these newer big-science projects, unlike the Human Genome Project, will not produce many results that are helpful to individual investigator-initiated research. And as long as they are sucking up pieces of that finite pie of research dollars, there will be insufficient government funds to support the backbone of science - the individual research grant, which is driven by the curiosity and vision of the individual scientist, not dictated by the top-down fiat of an administrator or the self-interest of some powerful cabal of senior investigators.

What's to be done? We as a community of individual investigators have to take back control of the scientific enterprise. Not administratively - believe me, you don't want that - but in terms of input into the setting of priorities. We need to demand that big science receives scrutiny as critical - and suffers consequences as severe - as our own grants do. We need to lobby our scientific societies to take firmer stands about these issues, and we need to help science administrators and policy-makers in Washington find the right way to phase out programs that should die, and explain to Congress and the people why this is the smart thing to do.

There is an alternative, of course: we could all jump on the big-science bandwagon. We could form teams to do even more huge data-gathering projects and encourage the government to put even more of its research dollars into such programs; after all, they would then be benefiting us. There's only one problem with that. If I'm right that this is a bubble, then some day that bubble is going to burst. There never has been a bubble that didn't.