Comment

The right to be wrong Gregory A Petsko

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The hardest promises to keep are the ones we make to ourselves. I promised myself that I wouldn't write about the presidential campaign this year, at least, not until the candidates from the two major parties were decided. I had no wish to add to the hot air generated by the bloviating political columnists and other self-appointed 'experts' whose constant presence is one of the biggest reasons I hate the protracted American primary process. I also didn't think anything I could say would have any connection to genomics. Yet, as I watched the campaigns for both parties unfold, a connection did occur to me - one that seemed not only to be ignored by most commentators but also to be surprisingly relevant. It has to do with the issue of 'flipflopping' - of changing one's position on an issue.

In the 2004 presidential election Republican incumbent George W Bush got a lot of political mileage by painting his Democratic challenger, Massachusetts senator John Kerry, as a 'flip-flopper' on the issue of the Vietnam War. Kerry had fought, honorably, in that war - a war that George W Bush had managed to avoid participating in by virtue of family connections. But after returning to the US, Kerry decided that the conflict had been a tragic mistake and he spoke out against it at numerous rallies. So successful was Bush's campaign rhetoric in portraying Kerry as someone without principles, that a large segment of the voting public came to believe that the decorated war veteran was less patriotic than the man who had never fought at all, an example of 'doublethink' that George Orwell would have been proud of.

The primary campaign this year has seen the same tactics employed, this time by the Republicans against one of their own. Mitt Romney, the former governor of Massachusetts (what is it about candidates from my home state?), saw his candidacy go down in flames largely because he was shown, truthfully this time, to have changed his position 180 degrees on such insignificant matters as gun control and abortion rights. In contrast, his opponent, John McCain, successfully presented himself as a man of unwavering

principle (even though he did a series of about-turns on the Bush tax cuts for the wealthy and several social programs).

The Democrats aren't immune from the problem either. New York senator (and former First Lady) Hillary Clinton, has shown impressive grasp of the issues and political savvy in debates against her chief rival for the presidential nomination, the eloquent senator from Illinois, Barack Obama. But she has spent much of her time trying not to apologize for her vote in the Senate in favor of the resolution that gave George W Bush the license to go to war in Iraq. She was lied to, of course, just like the United Nations and the American people were - there never were any weapons of mass destruction and Saddam Hussein had no connection with Al Qaeda or the terrorist attacks on 11 September 2001. So she certainly has every excuse, but she seems utterly unable to admit that the vote was a mistake. It's as though she were afraid to use the word.

When did admission of error become a mortal sin in politics? Many Americans believe that George W Bush is a great president because he has never admitted to making a mistake, has never changed his mind about any of the things he has professed, has never wavered in his convictions no matter what the evidence shows. (Of course, many Americans also believe that the Earth is 5,000 years old. Come to think of it, George W Bush is one of them.) To hold to your ideas when the facts show they are wrong isn't noble or steadfast, it's stupid. Yet, somehow we've come to equate closed-mindedness with toughness and integrity.

All of which would have nothing to do with science in general, or genomics in particular, except that I think it does. The worst thing that can happen to a scientist is to publish something that turns out to be wrong. It can wreck a person's career. All of us live in fear of it. And yet, should we?

So often we don't seem to make any distinction among types of error. I think there's a huge difference between sloppiness

and honest mistakes, between bad experiments and naive interpretation, between a failure to do controls and promulgation of a theory that turns out to be wrong. In each case, the former is much worse than the latter, but we often make little distinction between them in terms of the consequences to the unfortunate individuals involved.

It's hard to do perfect experiments. Nature takes a perverse delight in finding ways to fool even the most diligent experimentalist. Only someone nervous to the point of paranoia is likely to go through their entire career without misinterpreting some result or overlooking a trivial explanation. When the refereeing process works as it should, such mistakes can be caught before publication, but many journals, particularly the vanity press, don't insist on enough experimental detail to make that process work as it should (and sometimes one wonders about their stable of reviewers, too).

It's also easy to fall in love with a hypothesis, and to hang onto it longer than the data say you should. These aren't good things for a scientist to do, but they shouldn't result in capital punishment. Yet, when funding is tight and competition for journal space and important discoveries is keener than ever, the temptation is to magnify the mistakes of our rivals, to exaggerate their 'wrong' conclusions and trumpet the deficiencies of their work. Which makes everybody even more afraid of making, or admitting to, a mistake.

The result of all this, of course, is a climate of fear, entrenched positions and conservative science. Funding agencies - and grant reviewers - don't want to be accused of supporting work that is incorrect, so they reward the incremental, safe projects at the expense of the bold and risky. Scientists don't want to be pilloried by their colleagues for having made a mistake, so they tend to do the incremental, safe projects and eschew the bold and risky. And those who do slip up are often punished far out of proportion to the real import of what they have done.

I worry that a significant component of the current enthusiasm for data-gathering, as opposed to hypothesis-driven, biology stems from this climate. 'Discovery-oriented' research seems much safer: so long as you get the sequence right, or the crystal structure right - so long as you deliver the mass of data that you promised - you can't make a mistake. With only obvious conclusions to draw from those data, errors of interpretation are practically impossible. And data gathering usually doesn't involve clever experimental design that requires numerous controls to avoid artifacts. Funding agencies love it because they can point to tangible results that are always 'correct'. If we're not careful, our rush to punish those of us who make mistakes may turn some of the best of a generation of scientists away from the difficult, but essential job of trying to figure out what all these data really means.

I think what is needed is a decriminalization of certain types of error. Of course it's right to condemn sloppy experiments, missing controls and unwarranted conclusions. But we should encourage the scientist who takes sensible chances, who is not afraid to do the unfamiliar, and whose theories challenge the accepted dogma when that dogma fails to explain all the facts. And we should not condemn him or her when, as will often be the case, those chances misfire and those explanations turn out not to be the answer. And we should not be afraid to abandon our chosen explanations and hypotheses when the preponderance of the evidence goes against them. Nothing holds science back longer than this clinging to what should not be clung to, and all too often it's fear - fear of the consequences of having made a mistake - that keeps ideas around long past their sell-by date.

Closed-mindedness is a very bad quality in a scientist. Intellectual courage is a very good one, and if we continue to deny ourselves the right to be wrong, we run the risk of seeing it go the way it apparently has in politics

What would you think about a biologist whose motto was: "I shall try to correct errors when shown to be errors; and I shall adopt new views so fast as they shall appear to be true views." My guess is that you would applaud such sentiments as the hallmark of an open mind, one that was not afraid to change an opinion when the data indicated that a previous position was no longer supported by the available facts. It might surprise you, in view of this column, to learn that those words were written by a politician. His name was Abraham Lincoln. He would have made a heck of a scientist.