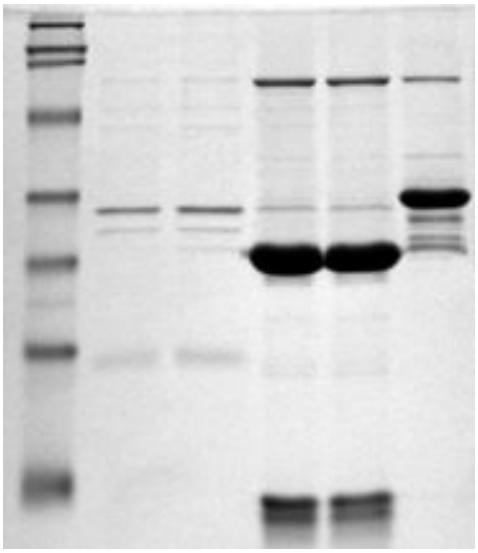
A joke no more.

Many years ago, when I was a graduate student, a friend and I came up with a "business plan" that we shared with the other students and post-docs in the department; they laughingly declared themselves desperate to invest in our sure-fire idea. At the time, both of us were running many gels and blots – a type of biochemical analysis in which the presence and molecular weights (sort-of) of proteins show up as lines of stain, as in the image to the right. They are an important mainstay of analysis, even more then than now, but they are very boring to run and can go wrong in an irritating number of ways that have nothing to do with deep scientific principles and everything to do with the physical problems of keeping liquids and high-voltage electricity where they are meant to be. At the time of our plan, we still photographed these things on real film, and labelled our photographs using rub-down letters and arrowheads made by *Letraset*, rather than by imaging and annotating digitally, as is done now. Our "business plan" was to save everyone the pain of late-night blot running by producing *Letrablot*^{TM} ; sheets of rub-down bands researchers could place wherever they wanted them. It was a joke, of course, made by tired grad students watching their blots run in the dark hours. The fact that we were there thinking up such silliness as Cambridge bells tolled midnight and blotting apparatus bubbled away on our benches was clear testimony that our hearts lay with real science, painful as its progress can be, even if our sense of humour was on the mischievous side.



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Until a few hours ago, I still thought the joke funny. Then I read my copy of this week's Times Higher Education (a sort of academics' trade magazine), and the smile has faded. There was a small news piece about fellow Edinburgh academic, over in the Faculty of Science, whom I have known in an occasional-chat-over-coffee way for many years. The article said she had been dismissed for Research Misconduct – for publishing falsified results – and that the university is seeking to have the journals involved retract her affected papers. The news came as a complete shock, all the more so because I have never been one to connect to networks of gossip so had not heard even a hint of the scandal. I confess I am still struggling to accept that she could have done what she has been

alleged to have done, which amounts to ia modern variation on our old joke of *Letrablot*™, done for real.

Everything is so public there is no point in my avoiding using my (ex-)colleague's name, and being opaque might run the risk of a reader guessing and misidentifying the person about whom I am writing, so I will be clear: the story centres on the work of the molecular cell biologist, Irena Stancheva. I will describe the alleged misconduct briefly here: more details can be found at the *For Better Science* site (see 'Links' below). The events revolve around four main papers, published in 2000, 2001, 2003 and 2004, with a fifth in 2005 partly affected. Each of these papers contains at least one figure from Stancheva that shows evidence of manipulations not described in the paper and which are, frankly, bizarre (ie not the kind of manipulation one might make routinely but perhaps forget to mention, for example adjusting the contrast of a complete set of images, experiments and controls treated the same way, to improve the way they look when printed). The images are gels and blots of the type shown at the start of this blog post (the one at the top of this article, and reproduced again here, is not from Stancheva's work but is a normal one from Wikimedia commons). In such an image, each band is produced by a real physical process, which is why they are blurry and wobbly compared to, say, barcodes on a supermarket label. Therefore, even when two vertical 'lanes' of the gel or blot contain identical proteins, as the 4th and 5th ones of the image to the right appear to, the images of the bands are not identical. Look, for example, at the slopes of the bands at the bottom; those above the word 'from' slope differently from those above the word 'Manske': really close examination shows other bands to be unique as well.

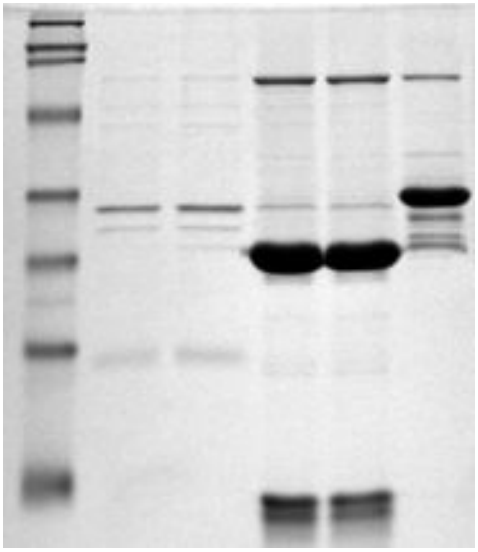

Image credit: Magnus Manske, from Wikimedia Commons and used under the Creative Commons BY-SA3.0 licence.

Someone reading one of Stancheva's papers noticed that some bands or sets of bands seemed to appear more than once on an image, or appeared on two different images that were stated to be two different experiments. I do not have permission to copy the affected images to this blog, but I have placed a link to a typical analysis, showing annotated images, in the 'LINKS' section. Now, if the

appearance of one small part-image in two experiments in just one paper had happened, it would be embarrassing, but it could conceivably arise from bad data management rather than intentional malfeasance. One could imagine, for example, the images of controls from two different experiments each being given the filename 'control' without extra information in the file-name, and someone later getting confused about which image went with which experiment. Bad labelling of files should not happen but it is not unheard of, especially in an environment that includes inexperienced students. But, while having this happen once may be misfortune, twice can seem like carelessness and three times…

More significantly, it is very difficult to imagine *any* honest process that could result in a band appearing more than once in the *same* image, and that is what is shown in some of the analyses in the LINKS section.

I am not a natural policeman, and certainly not a judge, so I don't want to think any more about the figures in these papers, or about the dismissal, or about whether the whole incident was handled as well as it might have been (the author of the *For Better Science* article has raised some questions about the handling of it). What I do want to think about is why it might have happened, and why it might not have been spotted earlier.

In dealing with 'why' someone might falsify images, the first thing to say is that all the evidence is that Stancheva was ('is'! – it's weird how this news has made me reach for past tense) a technically and intellectually capable scientist. I base this not simply on remembering her contribution to university research meetings and conversations, but on the fact that one would have to be competent at the bench to obtain enough blot images to have the raw material to cut-and-paste to make the alleged falsified manipulated images. Also, she went on to publish many other papers (generally in a more senior, less hands-on role, judging by position in the authorship list) which have not been identified as being problematic. So we are not talking of someone pretending to have skills they did not have (like the basketball player masquerading as a pilot in the film *Airplane*, for example); everything points to the fact that she could have done the experiments properly, but chose not to. Why might somebody do that?

The most obvious explanation is pressure; not direct pressure from colleagues, necessarily, but a perceived pressure to publish as many high-profile papers in a short time as possible, to out-

compete other young scientists for positions and funding. Obviously the moral and ethical position is that no scientist should fabricate data, whatever the pressure, but there is no reason to assume that scientists, as a group, are any less prone to temptation than other people. The entrance requirements for science are based on intellectual and technical ability, and (at least in the West) nobody tests moral rectitude. And, even among the morally righteous, it is conceivable that someone with a strongly consequentialist set of personal ethics might justify fraud early in their careers if it gets them a position that lets them to a great Good, such as curing a terrible disease, later on. I stress I am not making this argument myself (my personal ethics lean more towards deontology than consequentialism anyway), but I can see that it is an argument that could be made.

We scientists, as a group, are meant to be evidence-driven. There is a huge amount of evidence that, if one puts young people in a situation that is highly competitive and where the winners take all, even people thought to be above temptation fall. Think of sport, and how often sports-people found to be taking drugs to enhance their performances seem to shock their friends and relatives, who were sure that, while they knew drug taking is rife, their particular friend was morally strong enough to say ‘no’: to say ‘no’ even if that meant losing to someone else who was cheating. Yes, there will be plenty of sports-people who really do ‘play with a straight bat’, just as I still believe that most scientists are truly honest with their data, but the evidence from humanity in general is that intense pressure is not the best way to promote good behaviour. Furthermore, one might assume that, as with many other types of shameful behaviour, once one has committed scientific fraud once, doing it again will become both easier and even more necessary (necessary to meet the inflated expectations produced by that first apparently stellar performance).

I have already mentioned the pressures of competition but there has, in recent years, been another source of ridiculous time pressure exerted on researchers. When one sends a research paper into a journal, it is sent out for peer review and (usually) the reviewers reply with suggestions for improvement. Most editors treat these suggestions as conditions for acceptance. There is therefore usually a round of revision, which may well involve further experiments. In the last two decades, there has been an annoying trend for journals to demand that the paper be resubmitted within a short time, usually one month, or a resubmission will not be allowed. This creates intense pressure for someone, typically someone relatively junior, to perform experiments that would normally be developed over a much slower and more careful time-frame. The temptation to cut corners is high. The only time I have ever detected the possibility of substandard work from someone in my own

lab was in exactly this situation, when the person involved was suggesting an experimental response that would meet the letter of what was demanded, but not the spirit. I must stress that they were absolutely not suggesting anything remotely fraudulent, but were proposing to follow the precise instructions of the reviewer even though we both knew that the reviewer had not really thought these instructions through, and that our following them and doing nothing more would not really answer the question that was bothering him. I gently asked my colleague to consider for a moment that the reviewer might be right in his concern, and how stupid we would look if we did not properly check beyond doubt. I also reminded them that academic reputation is like virginity – once you lose it, you can never get it back (I do not usually use analogies as politically incorrect as this, but I wanted to make the conversation truly memorable because it was one of those moments when a lab head's words really can shape a young scientist's career). My colleague's momentary lapse was just that, and they did a superb job of nailing down the point two different ways. I am mentioning the incident because I view that person as highly trustworthy, and their momentary wobble was a vivid illustration of the unreasonable pressure they felt (from the journal, not from me – I would have been happy to tell that journal's deadline-obsessed editor to take a running jump and to send the paper elsewhere). I sort-of understand where this behaviour of journals has arisen: they fear if they give too long for revisions, a rival paper might be published first but they will still be honour-bound to accept the revision. This fear is, however, misplaced: if two papers are published that say the same thing, by rival groups, so much the better – which is first really does not matter, and the fact that they agree (assuming they do) make the data that much more certain. In practice, both will be cited together by subsequent authors anyway. As an Editor, I do not give these deadlines unless the only changes are trivial edits of text. I have no idea whether this particular thing about revision deadlines had anything to do with Stancheva's story, but it is one source of pressure we, as a community, can definitely remove, and we should.

None of the affected papers were published by Stancheva alone, and readers may wonder why her senior colleagues did not spot the manipulated figures. I think the simple answer is trust. We trust the people with whom we work. If we did not, why would we work with them? Would you work with people who do not trust you? I wouldn't. When we look at images of gels, blots etc., we concentrate our critical thoughts on the conclusions to be drawn, not on asking 'is this real or is it a fake?'. I really feel for the other authors of those papers, some of whom are now very senior and rather famous: I am sure each is wishing they had spotted the manipulations, but I very much doubt that I would have spotted them had I been part of the collaboration. You don't think that way, any

more than you think your colleagues are stealing from the petty cash. Having read this sorry tale, will I now be attending lab meetings and scanning every picture I see with “is this fraudulent?” the uppermost question in my mind? No – I will continue to supervise, advise and support folk in the lab as well as I can, and will try to create an atmosphere in which nobody feels under undue pressure to do anything other than their honest best. Then I will continue to trust them. Foolish? Maybe - but, like the choice of whether to check your life partner’s ‘phone and mail and movements or simply to take their fidelity on trust, it comes down to a question of how one wants to live.

Jamie Davies

August 2018

LINKS

The For Better Science account - https://forbetterscience.com/tag/irina-stancheva/ - this contains additional internal links to details.

A list of the papers affected - https://drive.google.com/file/d/0By2HqPi4t2RbZDBkVGxkM1dQMkxKM0JTWHJkTy1Cb1poZjNj/view (I found this via the For Better Science site, and have not verified it independently).

A typical analysis - https://pubpeer.com/publications/B683B717BB14E63B51F6CE26D74F8D