Keeping it real.

Just over a decade ago, one leading UK politician described another leading UK politician as *an analogue politician in a digital age*. The phrase was clearly intended to be an insult, but as an insult it makes no sense. Analogue representations of something (sound, light, voltage, barometric pressure etc.) follow that thing as faithfully as the technology allows: they are as close to reality as one can get. Digital representations, on the other hand, are only crude approximations of the analogue original: the process of making a digital signal begins with the analogue one and samples (measures) it repeatedly, creating a stream of digital numbers that effectively 'chunk' a smoothly-varying analogue input into a series of steps. The more often the conversion process makes measurements, the better it captures the information in the original analogue signal: sampling every Nth of a second will capture information that includes only frequencies almost up to 0.5N Hz (the Nyquist-Shannon criterion: see Links). Similar criteria apply to sampling across space, determining for example the resolutions of an image. The best a digital system can ever hope for is to be not very much worse than the analogue…to be not too crude a lie. That is why being *an analogue politician in a digital age* is really a generous acknowledgement of integrity. That it was intended, and was heard by the packed House of Commons and the public, as a withering put-down reflects a peculiar, almost Orwellian mantra of our times: 'digital good; analogue bad'.

I was reminded of this a few days ago in the lab, when a normally highly capable member of the team knocked at my door and said that they and a student had spent half an hour trying to get a wide-field microscope to work properly, and needed help. I positively like people giving me a reason to take a break from grant-writing to do something in the lab, so I followed them to the microscope very willingly. As I glanced at the indistinct image on the screen of the computer attached to the microscope, the researchers who had called me listed, far faster than I would possibly take in, all that they had tried altering in the settings of the computer system, to no avail. I wandered across to the microscope and did the one thing that, it turned out, neither of them had thought to do: I looked down the eyepiece. This simple, and to them amusingly old-school act, revealed at once that the image was terrible down the eyepiece too, exonerating at a stroke anything to do with the camera or the computer system attached to it. It was the work of only moments to realize that the sub-stage illumination system, which can be changed by a slider to from a transmitted light mode to a dark-field mode, was in some weird intermediate setting because something had knocked the slider: pulling the slider fully home into its 'transmitted' position generated the expected clear image.

The point about this story is not that I solved the problem quickly (anyone else of my generation would have been at least as quick; probably quicker). What I found interesting was that two highly intelligent, capable and creative young scientists had spent half an hour of their time *not* solving it, and that they had not solved it because they had concentrated their efforts entirely on changing the configurations of a programme running on a digital computer, attached to a camera, attached to the microscope. Nobody had thought to use their analogue eyeballs and just look at the real image. This was by no means an isolated incident, but is more the nature of a final straw that has led me to put fingers to keyboard. I have lost count of the number of times undergraduate project students, or occasionally more advanced students who really should know better, have called me in to a puzzling image on the screen of a fluorescence microscope. These microscopes are usually used to view cells that have been stained with fluorescently labelled antibodies that recognize a specific protein: the image shows where in a cell or tissue the protein is expressed. The camera and computer combination attached to the microscope can operate in many modes, and the usual starting one for a first look is ‘Auto’, in which the system will set its own exposure and sensitivity to generate some kind of reasonable image. There are then other modes that, for example, lock this exposure to be the same for all samples in a run of an experiment, to allow them to be compared. When I am called, the typical puzzle on the screen is an image that shows absolutely everything in a tissue to be stained, and the student concludes the antibody has no specificity. A glance down the eyepiece (typically still covered with its protective cap) usually reveals utter blackness instead of the image on the screen: what has happened is that the student has in some way messed up the staining so there is no signal at all from the antibody, and the computer running in ‘Auto’ has turned up the gain and exposure time of its highly sensitive camera until it can get an image from the very, very weak natural fluorescence of biological membranes. I am never irritated that the student’s attempt to stain failed (we all make mistakes), but I am baffled that they never bothered to look with their eyes, before turning to the computer.

Why does the screen have such a hold on people? Science is the study of the real world and, quite apart from there being good reasons to look at the raw data as a check, there can be a real thrill in seeing nature in a way that is as unmediated as possible. That is one reason that amateur astronomers shiver behind their backyard telescopes and peer up at frosty skies. A web search would bring up far more spectacular photographs of nearby planets or distant galaxies, taken by space probes or by orbiting telescopes, yet people still remember the thrill of seeing Saturn's rings for the first time in a blurry small refractor shaking in the wind. Ornithologists keep their lonely vigils on a salt marsh, getting glimpses of birds they would see in far more detail on the television or web, amateur geologists tap away at their rocks, and a host of other enthusiasts get real rewards from experiencing the wonders of nature in as direct manner as possible. When I am doing an experiment of my own, I look down the microscope first not just to check that all is well for the computer to see, but for the sheer pleasure of seeing the results with my own eyes. Why is this desire to be as close as possible to nature being lost from the new generation in professional labs? In an era of fake news and manipulated images, it seems doubly bizarre that the computer monitor should be the natural focus of someone intend on unearthing new truths.

I think me new-academic-year's resolution will be to try to focus lab folk on the most direct ways to view their experiments, with the fancy computer-controlled recording and analysis tools being a necessary and useful second step, but never a first one. Well, that's what I say I'll do but, as you are probably reading this on a computer screen right now, you should probably retain a healthy level of scepticism.

Jamie Davies
Edinburgh
June 2017

Links:

- Brief explanation of Nyquist-Shannon: https://en.wikipedia.org/wiki/Nyquist%E2%80%93Shannon_sampling_theorem