
News from the Essex Marches - or does British biochemistry have a future?

Peter Nicholls

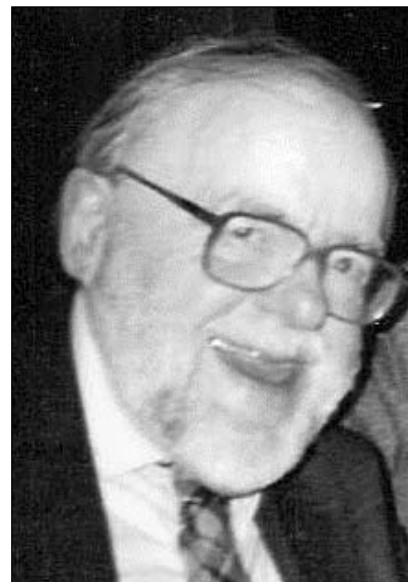
Visiting Professor of Biological Sciences, University of Essex, Colchester, U.K.
Emeritus Professor, Biological Sciences, Brock University, St. Catharines

In optics, Alhazen's problem is: "Given a light source and a curved mirror, find the point on the mirror where light will be reflected into the eye." Alhazen (Arabic al-Haytham), the author of a 7-volume work on optics 700 years before Newton, was probably the first to understand — in the year 1000 — that vision does involve reflection of light from object into eye (1). This non-intuitive idea had taken long to be established. Known as al-Basri from the city of his birth, Alhazen had begun a career as minister for Basra, but became disenchanted with religion and politics, and took up science and mathematics. Narrowly escaping execution for displeasing the Caliph, he spent a large part of his later life under house arrest like Galileo. The next serious advances in optics had to wait about half a millennium. Cultures can enter stasis, or decline, for reasons both internal and external. Could we be entering a twilight era of Western science?

Biochemistry in the 21st century will inevitably be different from that in the last century. Internal reasons already include changes in emphasis away from the metabolism of small molecules and towards the complexities of proteomics. When we step out of a time machine to meet students in 2100, if there are any, we shall amaze them with our knowledge of the minutiae of carbon chain metabolism (aka the Krebs cycle) while their computers may baffle us with a technical grasp of cell biology. A look at the complex descriptions of carbohydrate metabolism in the late 1930s made one appreciate the simplification created by Krebs' deep insights. But when I learned the cycle it was only 15 years old. 50 years have passed since then. Similar simplifications may be hidden within the

complexities of protein-protein interactions during the cell cycle. But I doubt it, though I hope to be proven wrong.

Biochemistry in the 21st century will also be affected by external causes. The well-documented retreat of undergraduate academic science, both in numbers of students opting for university courses and in types of course available, is accompanied by a governmentally-supported commercialisation of research. Funds are also increasingly targeted at an elite. We in the UK all compete for research funds departmentally, less individually than in Canada, and departments are graded in five or six categories from 1 to 5*. To be a 1, 2 or even 3 is to be unfunded and almost certain of closure; to be well-funded the RAE grade (2) must be 5 or preferably 5*; Essex is a 4.



The RAE for research is matched by a TQA for teaching (3). Both involve immense input of administrative time and effort. Imaginative (or ordinary) teaching is also threatened by a mountain of bureaucracy and paperwork. Decisions about student marking, procedures and extensions, which in Canada used to take a few moments, require official forms, records, meetings and decisions in committee. Outside social change means that biomedical and sports sciences are chosen

options rather than classical biochemistry. The trend to professional organizing and administration, seen most dramatically in government with most decisions and plans made by highly paid appointed technocrats rather than unpaid elected politicians, now extends to academia. The UK Biochemical Society abandoned its tradition of multiple meetings throughout the year, based in universities and free to all members, and replaced it with a single annual event (in Glasgow for the next 5 years) at a conference centre with professional organizers and a substantial registration fee. We hosted the last old style biochemical meeting in Essex in mid-2003.

Enrolment and funding declines have seen many university science departments closed. Essex has lost chemistry and physics, replacing the former with a multiplicity of biomedical courses and the latter by Electronic Systems Engineering. Biological Sciences seem safe because of our links to medicine, both theoretically and politically, with links to projects within the National Health Service and the prospect of becoming part of a new medical school.

In January 2005 the UK Biophysics Society and the Inorganic Biochemistry Discussion Group organised a meeting on protein mechanisms in Leicester. Leicester has Newtonian connections — his home at Woolsthorpe is not far — and a sundial Newton bust has just been placed in the university garden designed from his famous picture holding a prism. The work on light, following Alhazen's, was both physics and biophysics — his most dramatic experiment on his own eye involved pushing a bodkin behind the retina to show that it gave a sensation of colour. Newton died a long time ago and the Newtonian “research programme” (4) was abandoned for biology in the 19th century. This now is the year of Einstein, centenary of his three most revolutionary papers. But Einstein's method is about to join Newton's as a past way of thinking. *Nature*, in its Einstein commemorative issue (Jan 20th 2005), calls for his death to be accepted and for physics to “become” engineering (5), as has already happened here at Essex.

Steven Rose, biochemist at the Open University (appointed many years ago in a competition for which the writer was unsuccessful), is the establishment's gadfly. In a *Guardian* article (Dec 8th 2004) he linked the technocratic business orientation towards universities with the disappearance of socialism (6): “Building socialism may be a past dream but we could at least hope that New Labour could aspire to the broader vision of a science more accountable to the needs and concerns of civil society.”

Together with Ian Gibson (previously Dean of Biology at the University of East Anglia, now Labour MP for Norwich, government critic and chair of the House standing committee on science and technology), Rose keynoted a meeting in the House of Commons on January 19th. The occasion was the launch of a report by Scientists for Global Responsibility (7) on military involvement in science, which is not just a matter of nuclear weapons. It includes all hi-tech areas, including much electronics, and the US is now engaged in a massively funded research effort in 'Biodefence' — a grey area bridging defensive and possibly illegal offensive study of lethal bacteria, viruses and proteins. Rose himself was recently invited by the US military to collaborate (8). He declined. But one colleague here is cooperating with the Homeland Security-sponsored computer modelling of small-pox enzyme inhibitors, a project offered to the entire microcomputer-using world as a disseminated screen saver alternative to SETI under the unsubtle name of “patriotgrid” (9). It would be interesting to compare military and civilian R & D expenditure in the US and Canada with that in the UK.

The biochemical growth area of substantial pharmaceutical if not military interest in which our group is involved is the hormonal and cellular activity of nitric oxide. NO targets several heme proteins including both guanylate cyclase and cytochrome oxidase (10). NO generators, and direct and indirect (cGMP) target inhibitors, the most notorious being ViagraJ, are money spinners. And fortunately NO ligation is still a key to basic heme enzyme function and mechanism. But my

own most recent contribution combined traditional spectrophotometry and electron paramagnetic resonance (EPR) with the low temperature X-ray crystallography of formate-peroxidase (11). It is hard to make formate clinically or commercially relevant although it is responsible for binding liver catalase in one striking EPR-detectable symptom of death. The crystal structures were personally satisfying because they helped solve a problem I had as a graduate student (12). But in the drive to improve our RAE from a 4 to a 5 we are told that it is papers in *Nature* or *Science* that are essential. My own recent effort (13) sadly will not count.

1. Alhazen is at <http://www-gap.dcs.st-and.ac.uk/~history/Mathematicians/Al-Haytham.html>
2. The last RAE is at <http://www.hero.ac.uk/rae/> the next at <http://www.rae.ac.uk/default.htm>
3. The last TQA is at <http://www.qaa.ac.uk/revreps/reviewreports.htm>
4. Popper, K.R. & Eccles, J.C. (1977) *The Self and its Brain* (Springer International).
5. Editorial (2005) Einstein is dead. *Nature* 433, 179.
6. Rose at <http://www.guardian.co.uk/life/last-word/story/0,13228,1368972,00.html>
7. The report "Soldiers in the Laboratory: Military involvement in science and technology - and some alternatives" is a 560kb pdf file available at <http://www.sgr.org.uk>
8. Rose at <http://www.guardian.co.uk/life/last-word/story/0,13228,1393730,00.html>
9. Patriotgrid is at <http://www.3nw.com/pda/patriotgrid.htm>
10. Cooper, C.E. (2003) Competitive, reversible, physiological? Inhibition of mitochondrial cytochrome oxidase by nitric oxide. *IUBMB Life*, 55: 591-7.

11. Carlsson, G.H., Nicholls, P., Svistunenko, D., Berglund, G., & Hajdu, J. (2005) Complexes of horseradish peroxidase with formate, acetate and carbon monoxide. *Biochemistry*, 44: 635-642.
12. Nicholls, P. (1961). The action of anions on catalase peroxide compounds. *Biochem. J.*, 81: 365-374.
13. Lalanne, D., Nicholls, P. & Rotblat, J. (2005) Letter on nuclear weapons proliferation. *Nature*, 433: 571.