Let's Not Forget Plants

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My personal trajectory

I hated biology at school and gave it up as soon as I could, after a mere two years. It seemed to me – and this is nearly half a century ago – simply to be a question of labelling parts of plants and animals. I wanted to understand things, not merely be able to chant off a list of etymologically obscure words. Biology has certainly moved on a long way from its heyday of classification, although I fear school biology may have moved less far than the more advanced reaches of research. Perhaps if I were a teenager again I would make different choices, but I have never regretted sticking with physics.

As an undergraduate in Cambridge I was taught through the wonderful Natural Sciences Tripos. This, unlike most traditional UK science courses, would have offered me the opportunity to pick up some biology as well as carry on with physics because in the first year all students study three experimental sciences. This is, if you like, its USP and had I been tempted I could have studied Biology of Cells, a course designed (as I learned many years later) explicitly to tempt those with no biology background from school who wanted to understand cell machinery. But, given my lack of love for biology, it never crossed my mind to try it out for size. I stuck with the traditional physicist's trio of Physics, Chemistry and (as it was then called) Crystalline State, a topic which would now be termed Materials, as well as Maths.

A PhD on the electron microscopy of metals and a first postdoc at Cornell following on from that and there was still no biology in sight. I moved laterally from metals to polymers for my second postdoc at Cornell, continuing to use electron microscopy but now studying the failure of plastics. This wasn't driven by a sudden appreciation of why polymers might be more interesting than metals, or even a recognition that my spatial skills weren't up to visualising the complicated geometries of grain boundaries in crystalline materials. With hindsight both these statements were true but the motivation for switching fields was much more personal: I needed a job at Cornell to keep me in paid employment while my husband completed his PhD.

But it was this foray into the world of plastics that ultimately took me, after several more years, into something more biological. Or, in the first instance, a material at least of natural origin. Starch. Now once again I shouldn't imply great wisdom or foresight so much as pragmatism. I 'inherited' a major grant on food from a colleague who was returning to his home country. This grant, established along with Sir Sam Edwards (then the Cavendish Professor and head of department in Cambridge Physics), was a so-called 'linked' programme with the Institute of Food Research in Norwich. What is food from a physicist's perspective? It is of course, in many instances, polymeric. So I found myself moving from studying the failure of materials such as crash helmets to what makes snack foods crunchy? It's all about structure-property-processing relationships, in this case the key properties being mechanical strength and toughness. The snack foods I looked at were extruded: a mixture of maize and water put into the hopper and out of the other end came a foamed product whose properties depended on the thermal and mechanical energy input into the extruder as well as the composition of the initial mix.

To begin with I studied these unfamiliar materials with the traditional armoury of a physicist: electron microscopy and mechanical tests. How did the structure of the foam determine the strength or, as the foodies would have it, the 'mouthfeel'? You don't want to break your teeth on a Cheesy Wotsit, nor do you want it to crumble in your hands before you ever bite it. Getting the processing right to give you the texture you want is crucial for sales! We could use the Ashby-Gibson analysis of foams, developed in Cambridge's Engineering department, to study scaling laws and relate the size and shape of the cells in the foamed food to the end mechanical properties.

But there was something missing. If you extrude plastics you can change the size of the pores in the foam but basically the walls of the pores/cells are the same material. They may be thicker or thinner, the foam may have connections between the pores (an open-celled foam) or not (closed-cell), but the material is the same. That is not the case with starch. Depending on the processing conditions you may or may not break down the initial granule structure completely (granules are how the starch is laid down in the plant); you may or may not degrade the high molecular weight polysaccharide chains. The crystal structure that is present in the cells can also shift from one starch polymorph to another. In order to make sense of what was going on I had to understand the starch as a material better.

We turned to X-ray scattering to explore the internal granule structure. A lot was known about the crystal structure of the polysaccharides in the granule, but much less about the organisation at a larger lengthscale. So small angle X-ray scattering (SAXS) seemed a good candidate to use. The trouble with scattering experiments is that you need a model but my student was able to construct one which fitted the data well; not just the scattering data but microscopy data which showed that diurnal fluctuations led to so-called amorphous growth rings. The stacked lamellar of alternating crystalline and amorphous material sat in between these, with a repeat that turned out to be close to 9nm for every type of starch we looked at. This apparent 'universality' of packing caught the attention of biologists.

As it happened, this was just the time developments at the UK's synchrotron source, then at Daresbury, revolutionised the possibility of carrying out real time experiments combining different techniques. We studied cooking starch *in situ* using simultaneous small and wide angle scattering plus thermal characterisation via Differential Scanning Calorimetry. So we could watch the structure break down during heating and correlate changes at different lengthscales with thermal transitions. We could do similar experiments with neutrons where one had the additional tool of using 'contrast' by changing the amount of heavy water in the solution: hydrogen and deuterium scatter neutrons very differently so this provides additional insight as to what is going on as water enters the granule during heating and the structure breaks down.

By this point I had begun to get a reputation for this work. It was daunting to find myself deputed to make a presentation about the importance of neutron beamtime for biology to a funding agency which was considering whether such a relatively expensive technique should be supported by them. Me, a biologist? I certainly wasn't one and had still barely scratched the surface of biological processes; I was merely studying a natural material. Simultaneously, some of my physics colleagues were less than impressed that I worked with such unconventional and messy materials. The Cavendish Professor emeritus Brian Pippard made a scathing remark to me that hit me hard: *'Things have come to a sad pass when people at the Cavendish study starch*.' I think he felt that, having

devoted a lifetime to pure materials that could be completely characterised – such as his analysis of the Fermi surface in single crystals of copper – he could not understand why a physicist should want to study something so inherently complex as organic matter. Nevertheless, I am sure he was not alone in feeling I wasn't playing ball and that this simply wasn't physics. Sir Sam Edwards merely remarked 'physics is what physicists do', gave me every encouragement to continue and talked widely about my work with great enthusiasm. As a still relatively young lecturer, I needed this encouragement. Moving out of the straight and narrow is never easy.

So far the work had been carried out in a collaboration with the Institute of Food Physics and (the now-defunct) Dalgety-Spillers company but I would not claim by this point what I was doing was Biological Physics (or Biophysics, whatever label you want to attach to it). Now I turned to plant scientists for advice. Why was the 9nm repeat ubiquitous across species? First I turned to Tom ap Rees, head of the Plant Sciences department in Cambridge. He it was who pointed out how useful it would have been for me if I'd studied Biology of Cells as an undergraduate, how it was made for people like me, but this advice came at least 15 years too late. More importantly he pointed me in the direction of an ex-student of his, Alison Smith at the John Innes Centre in Norwich, a contact that formed the basis for a fruitful collaboration over 10 years or so.

Alison is a renowned plant biochemist concentrating on the study of starch synthesis. When we first met we got on very well at a personal level, a feature that I think is often overlooked when considering which collaborations 'fly' and which do not. At a scientific level we had to work rather harder at making things work. We spoke completely different languages. It is hard for a physicist to remember that things we take for granted – Bragg peaks in diffraction patterns being a case in point in our particular conversations – are alien and hard to get to grips with for a biologist. Conversely, the language of organelles and signalling were very unfamiliar to me and I felt confused and out of my depth. If a collaboration such as this is to work, it takes time. Sometimes, a lot of time. Much later I remember being told by another biologist that it had taken them two years of discussion with a physicist to establish sufficient common ground even to start to move the research jointly forward.

That collaboration with Alison was a joy; we both learned a lot and had fun working together. We never completely solved the 9nm puzzle but we had done enough to know it had to be physical rather than biochemical in origin, as I had originally naively assumed. We published a number of papers in different sorts of journals. But there came a point when I felt I had done what I could with starch with the tools I had. That point was reached at a conference when someone from industry kindly offered me 100 mutant starches to study. I knew that by that point I would not learn anything new from such a set, although I could come up with a spreadsheet of all the relevant parameters for each starch. It had ceased to be cutting-edge physics and could have begun to look remarkably like stamp-collecting, to use Rutherford's uncompromising language.

Further forays into biological physics were much easier but often also slightly accidental. My work on proteins grew out of an electron microscopy project studying protein aggregation of whey proteins – still on the food theme – but ended up exploring a whole range of different proteins. As a physicist I want to look for general themes rather than focus on the specifics of the amino acid sequence, for instance. The technique I was using (environmental scanning electron microscopy, ESEM) allows imaging of samples while they are still hydrated and without the application of any conductive coating. This significantly reduces the chance of introducing artefacts during sample preparation and

also, up to a point, allows dynamic processes to be followed. But electron beam damage remains a major concern. We explored which biological samples would be amenable to this approach. Our work showed that mammalian cells are unlikely to remain viable upon imaging but plant tissue is much more robust due to the different nature of its cell walls. Bacteria sit somewhere in between. However, despite all the hard work we put in on developing ESEM for biology, the simultaneous and rapid emergence of so many different kinds of super-resolution optical microscopy means that I don't believe ESEM will be the major player in the field of biological imaging I had once imagined. Nevertheless, this was another area where we had lots of fun working with interdisciplinary teams to see how far we could push things.

Perspective:

I mentioned that I met with some incomprehension verging on hostility when I started working on biological material from some physics colleagues. I think the changing face of physics – where complexity and emergent properties have become a central part of our thinking – means that such resistance would be less likely to occur now. Many physicists see the interface with biology as an exciting place to be. However, not all universities - certainly in the UK - teach much about this to their undergraduates, still focussing on fairly traditional areas of condensed matter. Even soft matter, the tradition out of which my own research grew, is often not taught or appreciated. This absence of exposure in the undergraduate curriculum is a serious deficiency in my view.

It doesn't take much to introduce some biological examples into standard courses, if that is all a lecturer feels able to do. For instance, in my first year undergraduate course on Waves and Matter Waves, I make sure I talk about X-ray diffraction from biological samples (DNA and proteins) when I discuss diffraction. I also use the video that Joe Howard and team produced of the wave-like motion of bull sperm: it's much more interesting than the classic and slightly artificial 'waves on a string' that physicists typically use as illustration. It's such a simple thing to do to sneak in examples that remind students that the laws of physics apply equally to living matter as to the more traditional inert stuff. Too often, British students can leave university unaware (as indeed I was in my own undergraduate days) of the richness of the situations in which we can take familiar physics concepts into the realms of biology.

To compensate this lack, a group of us in the UK with the help of the Institute of Physics, have produced some teaching material (freely available upon registration here http://biologicalphysics.iop.org/) which should help rectify the situation. Powerpoint slides and lecture notes are there to help those with less familiarity with the material slip some examples into a standard course – or indeed give a full module on some aspect of biological physics. With so much going on in the field, with the boundaries blurring between disciplines and interdisciplinarity finding favour with funding agencies, we need to make sure that students get the necessary exposure to the basic ideas.

However, I believe in the UK we have a further problem and that is around funding. Although funding agencies do talk up the idea of inter- and multi-disciplinary working, there are still problems where too much potentially exciting research falls through the cracks. My own suspicion is that this situation has got worse (whatever the rhetoric) as funding gets tighter. It is too easy for each agency to retreat to its 'core competences' and work that crosses boundaries between different funders is particularly likely to falter. There are opportunities round specific calls (e.g. biomaterials or

regenerative medicine). Nevertheless, many fertile but untargeted areas and collaborations can find it very hard to obtain funding.

My own trajectory into this field of biological physics was via what is now known as soft matter physics. The tools I use are still very much those from that background. There are so many opportunities, though, for physicists to get stuck in at the interface with biology. The world has moved on from where I saw it 15-20 years ago where very often physicists were called upon by biologists more to act as a service (often specifically an imaging service) to utilise some technique on a biological sample rather than as part of a genuine collaboration. Nevertheless I still see the world of plants as something of the poor relation in these collaborations. Far more physicists are involved in work on mammalian cells, bacteria or population and evolutionary dynamics than on getting to grips with plant science. In terms of food security – and sustainability more generally – this probably needs to change. The opportunities– and potential excitement and fun – are immense.