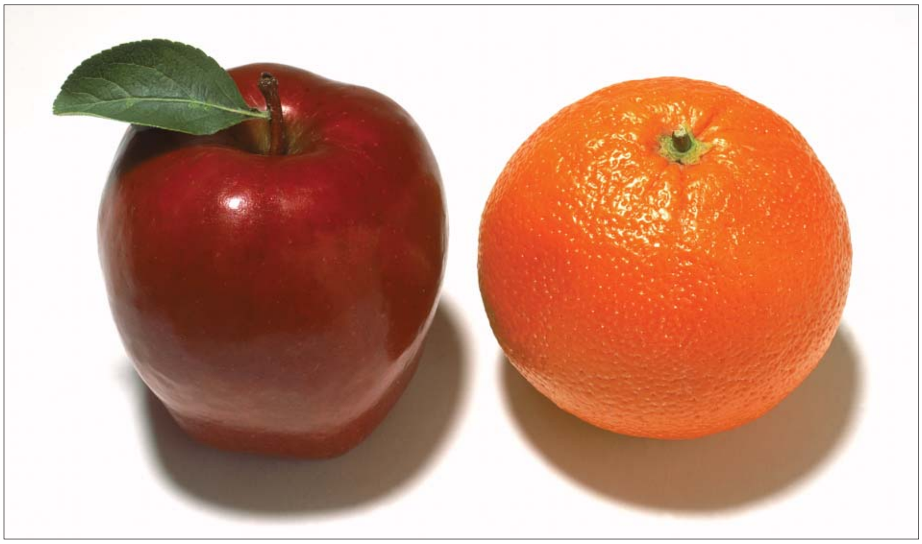
How physics can inspire biology

Alexei Kornyshev thinks that physicists and biologists are now working more closely together than ever before, but that barriers to closer collaboration still exist



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The same but different Physicists and biologists need to learn to better understand one another.

In July 1997 Adrian Parsegian, a biophysicist at the National Institutes of Health in the US and a former president of the Biophysical Society, published an article in *Physics Today* in which he outlined his thoughts about the main obstacles to a happy marriage between physics and biology. Parsegian started his article with a joke about a physicist talking to his biology-trained friend.

Physicist: "I want to study the brain. Tell me something helpful."
Biologist: "Well, first of all, the brain has two sides."
Physicist: "Stop! You've told me too much!"

Parsegian went on to list a few areas in biology where input from physicists is particularly welcome. But his main conclusion was that physicists must really learn biology before trying to contribute to the field. He also warned that it may not even be enough for a physicist to have a biologist friend to act as an "interpreter" to translate a problem into the language of physics.

Despite being gentle and elegantly written, the article provoked a stormy reaction from Robert Austin, a physicist at Princeton University, who accused Parsegian of forbidding physicists from tackling the big questions in biology. My view lies somewhere between those of Parsegian and Austin, and, in my opinion, the relationship between physicists and biologists has improved on some fronts in the 12 years since Parsegian's article first appeared. However, I believe that those relationships are still being poisoned by a number of misguided beliefs that are preventing physicists and biologists from working closer together.

More than beliefs?

Back in the early 1970s, when I was a first-year PhD student at the Frumkin Institute in Moscow, I used to attend theoretical seminars chaired by Benjamin Levich – a former pupil of Lev Landau – who was widely regarded as the founding father of physical-chemical hydrodynamics. Whenever an overly enthusiastic speaker would tell us with 100% confidence how, say, electrons and atoms behave in a solvent near an electrode, Levich would spice up the seminar by joking "How do you know? Have you been there?"

Almost four decades on, physicists now have plenty of experimental tools to "go there". For example, modern X-ray synchrotron sources allow researchers to look at how crystals form, to discover how biological samples mutate and even to pinpoint where ions adsorb on DNA; while techniques such as the fluorescence imaging with nanometre accuracy (FIONA) allow the motion of proteins such as myosin or actin to be traced in real time. But although these techniques often produce fascinating results, they may not be enough without a deep theoretical analysis of what one is actually "seeing". So, the first of these misconceptions is that "seeing is believing". A pretty picture may have a beguiling charm, but on its own it is not enough.

The second belief hampering collaboration is that the formalism of a biological theory must be simple – it should not contain more than exponential functions and logarithms (no Bessel functions, please!). Otherwise, the job should be left for computers to do. This point of view was advocated by Rob Philips of the California Institute of Technology, who came to his new love – biology – from solid-state theory. I strongly disagree with that view, however, and I used to argue with him about it when we were both on sabbatical at the Kavli Institute for Theoretical Physics in Santa Barbara. As I used to point out, James Watson and Francis Crick could never have deciphered the structure of DNA from the X-ray scattering patterns obtained by Rosalind Franklin and Maurice Wilkins had they not had the mathematical tools developed by Crick, William Cochran and Vladimir Vand a year earlier (1952 *Acta. Crystollograph.* **5** 581). Indeed, Bessel functions were at the heart of that analysis.

The third belief is that biologists will never read scientific papers containing mathematical formulas. As Don Roy Forsdyke, a biochemist at Queen's University in Ontario, Canada, once told to me, "The biological literature is vast. Biologists have too many papers to read and too many experiments to make. They will leave aside any reading that looks difficult." If this is true, and I think it is, physicists are in big trouble.

This brings us neatly to the next belief, which is that it is impossible for physicists to publish a serious theoretical paper in a biological journal. Theorists need mathematical derivations to validate their findings, but any paper containing derivations will be rejected. If you then publish the article in a physics journal, it will not be read by those to whom it is addressed. Actually, good papers of that kind are still sometimes published and read, but this remains a difficult issue.

DNA revolution

Physicists want to simplify and unify things, as much as possible, whereas biologists resist the reductionist approach and are happy with diversification and complexity. So, the biologists' fifth belief is that physicists are too ignorant about diversity to offer them anything useful. Biologists admit that physicists can provide, say, a new spectroscopic technique or apparatus for measuring forces, but that is about it. In their view, biology should be left to the professionals.

The final belief is that biologists think physicists made one big breakthrough – elucidating the structure and function of DNA – but that a similar revolution is unlikely to ever happen again. However, the key to that discovery was the "chemistry" between Watson (a biologist) and Crick (a physicist), which helped them to find a common language and gave rise to the idea of DNA replication and the subsequent principles of molecular biology.

I believe that we can expect other breakthroughs of this sort because physics and mathematics have a long history of revolutionizing not only science but our lives too.

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Meaningful collaborations

In spite of all this, my feeling is that physicists and biologists are getting on better. For example, last month, together with Parsegian and Wilma Olson of Rutgers University, who is another former president of the Biophysical Society, I organized a conference entitled "From DNA-Inspired Physics to Physics-Inspired Biology". Attended by some 140 researchers, the meeting was held at the International Centre for Theoretical Physics (ICTP), in Trieste, Italy, and sponsored by the ICTP and co-sponsored by the Wellcome Trust. But the conference was not just for physicists interested in biology. It was also aimed at biologists who were interested in learning what new physical methods and existing knowledge could offer them, as well as pinpointing for physicists the subjects that biologists think could benefit from input from physics.

The conference included over 60 talks – demonstrating the interplay between physics and biology – on everything from DNA mechanics, structure, interactions and aggregation to DNA compaction in viruses, DNA-protein interaction and recognition, DNA in confinement (pores and vesicles) and smart DNA (robotics, nano-architectures, switches, sensors and DNA electronics). More details are available online.

Taking Rutherford's famous saying that there is physics and everything else in science is stamp collecting, Paul Selvin, a physicist at the University of Illinois, recently said that if Rutherford were alive today, he would have said that "all science is either biology or tool-making for biology or not fundable". Today, in general, the arrogance is rarely on the side of physicists. But to overcome the barrier of scepticism, physicists need to demonstrate (or, even better, inspire biologists to show) that insights from physics do not just apply in model systems in the lab but work equally well inside the real world of the cell.

Crick not only had a great mind and was very serious about biology but he was also lucky to meet the right collaborator in Watson. Many of us seeking to do important work in biology will not be able to do so alone unless we too find the right match. The future is far from hopeless – and meetings such as the one held in Trieste last month may well make the difference. As the Cambridge physicist Stephen Hawking once said, "The greatest discoveries of the 21st century will take place where we do not expect them." Likewise, I am convinced that great surprises and discoveries in biology will come from physics.

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