

## Frontispiece to reprinting of 'Applications of magnetic nanoparticles in biomedicine' by Pankhurst, Connolly, Jones & Dobson.

In retrospect it is funny to recall how reluctant we were when first approached by the J. Phys. D commissioning editor, Kevin O'Grady, with the idea of contributing to a set of review articles on biomedical applications of magnetic nanoparticles. It was a novel concept to have not just one article but three, written by different groups, and covering, in turn, the synthesis of magnetic nanoparticles, their biomolecular functionalisation, and – in our part – the underlying physical principles of their application in biomedicine. It seemed like a curious way to encourage multi-disciplinary R&D – by separating out the chemistry, biology and physics into discrete parts – but Kevin was a persuasive advocate, and we agreed to give it a go.

It turned out to be rather liberating to be asked to focus on the physics. We set out to provide an easy-to-read resource for non-experts, and as such started by reviewing some of the relevant basic concepts of magnetism, including the classification of different magnetic materials, and leading on to a description of superparamagnetism. This was not as easy as we had expected – and gave us an appreciation for the work that goes into writing good textbooks. We went on to describe how a magnetic field can exert a force at a distance, and the physics of magnetic actuation. This section turned out to be something of a compromise between clarity and complexity, in that we did not go into as much detail as we'd have liked – for example to draw out the 3x3 tensor nature of the  $\mathbf{m} \cdot \nabla$  operator – so as not to scare off the reader. We then described the way that energy can be transferred from an excitation field into a magnetic dipole, and how this can be harnessed via magnetic field hyperthermia. Lastly, acting on a last minute suggestion from the editor, we attempted to demystify the physics of magnetic resonance imaging (MRI), and the role of magnetic nanoparticles as MRI contrast agents. This turned out to be challenging too, as we found out when we asked an MRI expert colleague to read and comment on our description, and the best he could say was 'well, it's not how I would put it, but at least it's not wrong'. Faint praise indeed, but looking back on it, our description, despite being so simplified, does seem to have served our purpose well.

Not everything went well on the physics side. We had a rude awakening when, in 2014, we found ourselves the subject of an internet blog post by Douglas Natelson entitled 'Bad physics as a marker for tracking text recycling'. At the heart of this was a sentence in the introduction to the article that read 'Second, the nanoparticles are magnetic, which means that they obey Coulomb's law, and can be manipulated by an external magnetic field gradient.' – which, on inspection, is at best enigmatic, and at worst just wrong. We had missed this at the proofing stage, and for a decade thereafter. It was the result of a botched shortening of a passage alluding to the magnetic Coulomb law as it relates to forces between acicular particles where the dipoles may be treated as well-separated monopoles – and was very embarrassing. Even worse was that Douglas pointed out that the phrase has turned up, verbatim, in subsequent publications by entirely independent groups and authors. We can only apologise for this, and hope that others will take it as a salutary message to always be assiduous when proof reading.

Returning to the article itself, the other main theme we explored, alongside the underlying physics, was the applications space, including prospects for translational advances in magnetic actuation, drug delivery, hyperthermia and MRI contrast agents. Looking back it seems that in 2003 we were on the cusp of a major expansion of both academic and commercial effort in these areas, and that the high citation metrics that the review received (more than 4,500 to date) owes a lot to this increase in activity in the ensuing years. It seems that once the physical principles were clearly laid out, new discoveries and applications came at a rapid pace.

That said, there remain very few examples of new magnetic nanoparticle applications finding their way into everyday clinical use – that is, beyond the pre-existing examples of MRI agents and *in vitro* magnetic immunoassays and bioassays. This most likely reflects the truism that it always takes much longer to bring a new technology to the market than you expect. Even so, there is some justification for optimism that the fruits of all the labour may soon be coming through. This is in part a reflection of the dedicated and sustained efforts that thousands of researchers have been making over the last 10-15 years – a significant fraction of many individuals' research careers – working in interdisciplinary teams with a focus on achieving real translational results. As a result of this work we now know much more about the ways that magnetic nanoparticles behave in the human body than we did in 2003, and we are much better able to control and manipulate them safely. A second cause for optimism is that dozens of new companies have been formed since 2003 with the express purpose of delivering the new applications into the healthcare market.

For this reason, we look ahead to the next ten years with both hope and confidence for the continuing growth and success of the field. Not everything that has been proposed or championed will find its way into clinical use, but more and more applications will successfully make the transition. Ultimately, given the unique properties of magnetic nanoparticles, and the many ways they can be exploited to perform safe and beneficial functions for human health, we think that that is the most important thing.

*Quentin Pankhurst, Stephen Jones & Jon Dobson*