NANOMATERIALS

# Viruses electrify battery research

A new approach to making battery electrodes with the help of genetically engineered viruses could reduce costs and improve environmental sustainability.

Jean-Marie Tarascon

Over the past two decades, the performance of rechargeable lithium-ion batteries has improved greatly[1], and these batteries now offer both high energy density (~200 W h $kg^{-1}$) and high specific power (~4.5 kW $kg^{-1}$). This performance makes them attractive for use in applications such as hybrid and electric cars, and solar and wind energy storage. Challenges to be overcome include lowering costs, improving safety and reducing environmental impact.

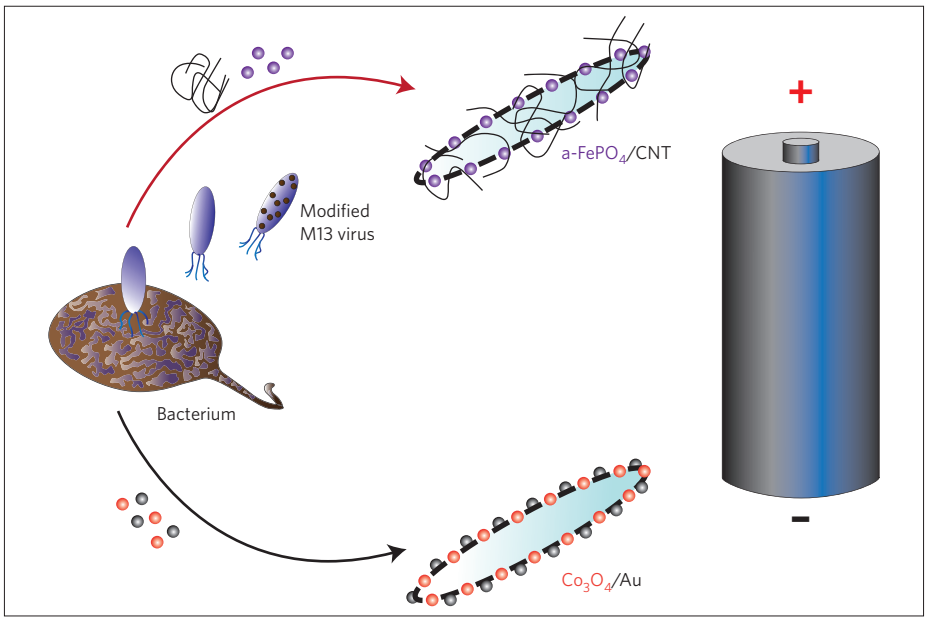
Lithium-ion batteries rely on the extraction of positive lithium ions from one electrode and their insertion into the other. Electrons flow at the same time in the external circuit. Research has focused on new electrode materials, and several cheap and abundant examples have been recently identified. These include iron-based phosphates and silicates, made from elements that are major constituents of the Earth's crust and are therefore practically unlimited in quantity.

There is, however, one important drawback to these otherwise attractive materials: their extremely low ionic and electronic conductivity. This can be partially addressed by using nanoscale materials to shorten the distances that the electrons and the lithium ions have to travel. Although the advantages of nanostructured electrodes are well understood, their rational design remains a key challenge for the chemistry and materials communities. In particular, a critical question for battery researchers today is whether nanostructured electrodes can be made by eco-efficient processes with a small carbon footprint.

Now in *Science*, Angela Belcher and colleagues at Massachusetts Institute of Technology (MIT) and the Korea Advanced Institute of Science and Technology (KAIST) report an elegant way of addressing some of these concerns[2]. Building on previous work in which they showed how a virus called M13 can be genetically engineered (Fig. 1, bottom) to provide a template for the growth of negative electrodes[3], Belcher and colleagues now apply the same biological principles in a new direction: the growth of a positive electrode based on amorphous iron phosphate (a-$FePO_4$). They find that engineering a single virus gene to nucleate iron phosphate results in electrodes that have acceptable capacity retention upon cycling but limited high-power performance. The common response of the battery community to such poor kinetics is to add an electronic conductor, generally a form of carbon, to the mix. Two of the most popular approaches are carbon nanopainting, which gives a thin coating of carbon to the electrodes, and the mechanical addition of carbon nanotubes. Although nanopainting produces a better interface than carbon nanotubes, it also requires high-temperature processing under a reducing environment, preventing its use for oxidizing materials such as ferric oxides .

It is here that the *coup de force* of the paper is found. Belcher and colleagues improve the performance of their iron phosphate electrodes with a new way of incorporating carbon nanotubes (Fig. 1, top). They engineer additional genes so that the M13 virus acquires an affinity for single-walled carbon nanotubes, in addition to its ability to nucleate amorphous iron phosphate. The resulting electrodes show much improved cycling properties, capacity retention and rate capability. Based on spectacular transmission electron microscopy images, the researchers argue that these improvements are the result of the high quality of the interface between the iron phosphate and the nanotubes. Moreover, the quality of the interface means that their electrodes can operate with a smaller amount of nanotubes (5% by weight), avoiding the incorporation of inactive nanotubes that serve only as dead weight, although this benefit is somewhat negated by the presence of inactive viruses.

Undoubtedly, the significance of this work lies in its demonstration of a new direction for the design of nanostructured electrodes, which is more likely to inspire




D. LARCHER & J.-M. TARASCON

**Figure 1 |** Biomimetic electrodes for lithium-ion batteries. Belcher and co-workers have shown that genetically modified M13 viruses can be used to make negative electrodes based on $Co_3O_4$ nanowires and gold nanoparticles[3] (bottom), and positive electrodes based on a-$FePO_4$ nanowires and carbon nanotubes (CNT, top)[2]. This particular pair of electrodes could not be used together because a $Co_3O_4$ negative electrode requires a lithium-based positive electrode.

future work, rather than lead directly to the design of new electrodes for lithium-ion batteries, as some press headlines have implied. Indeed, it is unlikely that iron phosphate/nanotube electrodes, which are lithium-free, will be used in commercial lithium-ion batteries because at least one of the electrodes in these batteries needs to contain lithium. Lithium metal cannot be used for the negative electrode for reasons of safety and cyclability, and lithium graphite ($LiC_6$) is too reactive. ($LiC_6$ is actually formed at the graphite negative electrodes in commercial lithium-ion batteries, but it is safe because it is sealed from air and moisture inside the battery). Belcher and co-workers are therefore planning to investigate the virus-based growth of lithium-containing positive electrode materials which have been previously disregarded because of their poor electronic conductivity.

One such material, $LiFePO_4$, is currently considered among the most attractive of electrode materials[4], and electrodes assembled from $LiFePO_4$ nanopowders have already reached the marketplace. Proposing a biological approach to making electrodes that are already on the market may result in some scepticism, which could have been allayed by a more candid discussion of the limitations and drawbacks of the virus-based approach in ref. 2. Nevertheless, battery research needs bold new approaches, and the work of Belcher and co-workers should drive the community to think out of the box, and raise awareness of the benefits of biotechnology approaches.

Can we, for instance, make such biological electrode wiring universal and trick Mother Nature, turning minerals that are abundant, but that are commonly recognized as electric insulators, into battery electrode materials? Nature already, for instance, handily manipulates phosphate species, breaking the strong phosphorus–oxygen bond (DNA and ATP); and mother-of-pearl is an extraordinary organic–inorganic composite made in billions of tonnes every year. Can these materials and processes serve as the inspiration for future bio-inspired electrode materials? Although these questions lack a clear answer today, it is a certainty that, for reasons of sustainability, the way we make electrode materials and electrodes will change in the coming decades. Whatever the solution will be, it remains that the work by Belcher and colleagues marks an advance in the design of electrode materials. The synthesis of the electroactive material and its implementation into a working electrode occur at room temperature, and this is surely a good thing. ❐

*Jean-Marie Tarascon is at the Université de Picardie Jules Verne, 80039 Amiens Cedex, France.*
*e-mail: jean-marie.tarascon@sc.u-picardie.fr*

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TOXICOLOGY

# Testing in the third dimension

Experiments with a new three-dimensional model of liver tissue find that the toxic effects of nanoparticles are reduced when compared with tests that use two-dimensional models.

Molly M. Stevens

Cells reside in a three-dimensional (3D) environment in the body and they are sensitive to nanoscale topographical and chemical alterations. The varied landscape of ridges, posts and grooves in the extracellular matrix influences whether a cell will grow or die[1]. Synthetic nanomaterials, which also present a nanoscale landscape, hold enormous promise in biomedical applications, but assessing and predicting their potential toxicity towards cells remains a challenge.

Now in *Small*, Nicholas Kotov and colleagues[2] of the University of Michigan and Nico Technologies report a new 3D model of liver tissue for assessing the toxicity of various nanoparticles. The new culture model aims to bridge the gap between *in vitro* and *in vivo* testing of nanoparticles, and to improve the predictive power of *in vitro* screening procedures.

*In vitro* tests of the toxicity of nanoparticles on 2D cell cultures have helped describe fundamental mechanisms of how cells interact with materials. This method involves growing the cells of interest on a flat substrate and measuring their response to the test material using various colorimetric, fluorescence, protein and gene expression assays. The problem with these cultures is that they do not reproduce many of the complex cell–cell and cell–matrix interactions found in the natural 3D environment of tissues and organs, and this limitation frequently means that the results from these studies cannot accurately predict outcomes in animal experiments.

Three-dimensional cell cultures in the form of tissue 'spheroids' are routinely used in cancer and pharmaceutical testing and are expected to be effective models for toxicity studies because they could potentially approximate the *in vivo* tissue structure and cell behaviour more closely than 2D cultures[3]. Liver tissue spheroid models are popular because the liver is the main organ where drugs are metabolized and nanoparticles accumulate. However, the development of simple and reproducible *in vitro* liver toxicity screening models has been hampered by the lack of control over the dimensions and organization of liver spheroids. Because the functional bioactivity of a spheroid is closely related to its diameter, reproducibility is necessary if they are to be used to screen for nanoparticle toxicity.

As a scaffold for growing the 3D liver spheroids, Kotov and co-workers prepared a cell-repulsive transparent polyacrylamide hydrogel[4,5] consisting of highly organized and uniformly sized spherical pores with small openings on the top side, and sub-cell-sized porosity throughout the walls of the scaffold (Fig. 1). Liver cells are delivered through the small openings and after a few days of culture the single cells grow into balls of cells called spheroids that are eventually trapped in the pores. Obtaining quantitative data from such 3D cultures remains challenging, but the well-confined spheroids in this case means that the total number of cells is kept constant and so the effects of different nanoparticles on liver tissue could potentially be characterized. By controlling the size of the pores, it is possible to reproducibly form spheroids that are 100 μm in diameter and still maintain good transport of gas and nutrients throughout the scaffold. Hypoxic conditions, which cause cell death, are a common problem in other poorly controlled spheroid models.