The nanowires showed an extremely high light-emitting efficiency, higher than 87% for the iodide samples. Importantly, the researchers observed lasing emission at optical stimulation as low as 220 nJ $cm^{-2}$, with tunability of the lasing wavelength across the visible spectrum obtained by modifying the material composition (Fig. 1). Lasing from films[5] or platelets[6] of hybrid organic–inorganic perovskites has already been reported, yet the performance of these first prototypes was not optimal, possibly as a result of the limited crystalline quality of the materials used. The exceptional low lasing threshold of the perovskite nanowire lasers of Zhu and co-workers, lower than that of any other semiconductor nanowire to date, is a direct proof of the significant reduction of structural defects obtained with the growth approach used; in fact, optical losses due to scattering or to imperfect reflections of the mirror end-facets are strongly attenuated.

A complete understanding of the growth mechanism of these nanowires will require further investigation. Although imaging by means of transmission electron microscopy would provide direct confirmation of the screw-dislocation-driven growth, such analysis has proved challenging because perovskite materials are unstable under the electron-beam irradiation conditions required by this technique. Hence, alternative approaches will have to be used to validate the one-dimensional growth model proposed by these researchers. In addition, a complete rate equation model describing the photophysical processes taking place in these perovskite materials may help to improve our understanding of the threshold behaviour. Last, the demonstration of electrically injected lasing will require the development of fabrication strategies and device architectures that minimize the detrimental increase of optical losses, which are due to the deposition of metallic contacts on the cavity.

It is interesting that these ionic perovskite materials seemingly have optical properties that are comparable to classic covalent semiconductors such as gallium arsenide. However, this ionic character also contributes to their sensitivity to air and moisture, and is likely to limit their potential application in advanced photonic circuits if this stability issue is not addressed. Yet the exceptional performance reported by Zhu and colleagues has already put hybrid organic–inorganic perovskites at the forefront of laser research. ❐

*Anthony Fu and Peidong Yang are in the Department of Chemistry, University of California, Berkeley, California 94720, USA, and the Materials Science Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, USA.*
*e-mail: p_yang@berkeley.edu*

## References

1. Yan, R., Gargas, D. & Yang, P. *Nature Photon.* **3,** 569–576 (2009).
2. Zhu, H. *et al. Nature Mater.* **14,** 636–642 (2015).
3. Green, M. A., Ho-Baillie, A. & Snaith, H. J. *Nature Photon.* **8,** 506–514 (2014).
4. Dasgupta, N. P. *et al. Adv. Mater.* **26,** 2137–2184 (2014).
5. Deschler, F. *et al. J. Phys. Chem. Lett.* **5,** 1421–1426 (2014).
6. Zhang, Q., Ha, S. T., Liu, X., Sum, T. C. & Xiong, Q. *Nano Lett.* **14,** 5995–6001 (2014).

IMPLANTED MATERIALS

# Larger is stealthier

Implanted spheres with a diameter larger than 1.5 mm escape fibrotic responses, thereby extending the survival time of the encapsulated therapeutic cells.

Ruud A. Bank

The immune system recognizes implanted materials as foreign, triggering an orchestrated series of sequential events that are collectively known as the foreign body reaction (FBR)[1]. The outcome of a FBR is the complete elimination of the implanted material via degradation or, alternatively, via the generation of a fibrotic capsule that shields the material from the body. Because of an ageing population, there is an increasing demand for tissue implants and implanted delivery systems, which calls for increased efforts to better understand the FBR. Harnessing the FBR is of considerable importance to successfully design biomaterials that attenuate fibrotic responses (so as to improve the half-life of the implant)[1,2] or that allow for a precise control of their degradation rates (and hence the formation of new tissue). Writing in *Nature Materials*, Daniel Anderson and colleagues demonstrate with a series of straightforward experiments a surprisingly simple solution to circumvent the unwanted fibrotic encapsulation of implanted spheres[3]. They show that the size of implanted spheres determines the extent of the body's fibrotic response, with bigger spheres triggering a lower FBR (Fig. 1).

Implanted spheres can be used for drug- or cell-delivery applications, for example, to host cells that secrete clinically relevant drugs (such as insulin). Yet, the injection of microspheres in tissues normally results in inflammation, a process that involves the recruitment of macrophages and fibroblasts as well as the macrophage-triggered activation of the latter. This results in myofibroblasts capable of producing a fibrotic capsule of densely packed collagen around the implant that hinders the release of drugs, thus impairing the implant's function.

Anderson and co-authors found that spheres with a small diameter (0.5 mm or less) implanted in mice, rats or monkeys elicited a severe fibrotic response, whereas larger, 1.5-mm spheres hardly induced capsule formation. Also, they observed that such a size effect persisted across a diverse range of materials, including alginate, stainless steel, glass, polycaprolactone and polystyrene, and that it was not restricted to a specific tissue (the authors injected the spheres subcutaneously or in the intraperitoneal space). Moreover, the size effect was restricted to spherical shapes, as increasing the implant size without taking the spherical geometry into consideration provoked fibrosis or rejection.

The mechanism behind such an apparently universal phenomenon is not clear, however. Anderson and colleagues observed minimal cell numbers (neutrophils, macrophages and myofibroblasts) on the surface of the larger spheres as well as little activity in the movement of these cells from the surrounding tissue to the larger implanted spheres (these experiments involved real-time tracking of fluorescent macrophages[4] in genetically modified mice). The opposite occurred for the smaller, 0.5-mm-sized spheres. They also observed differences in

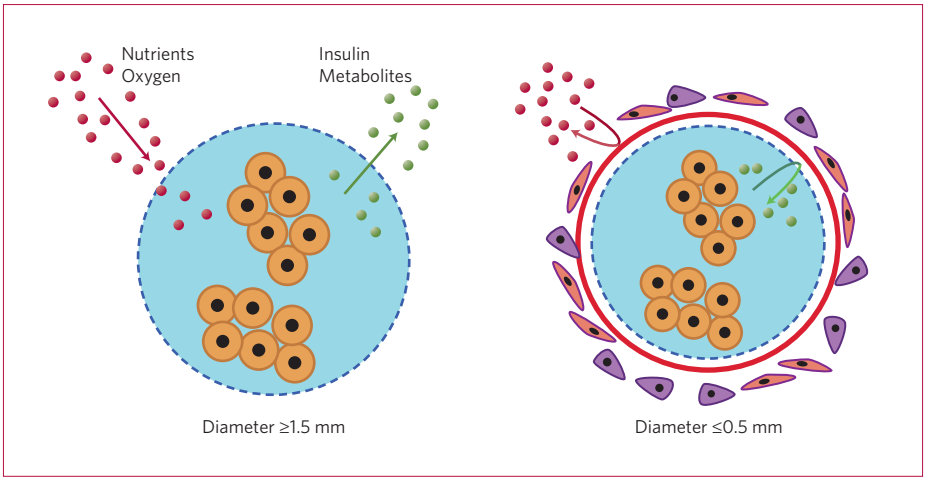


**Figure 1 |** Foreign body response to alginate spheres encapsulating insulin-producing islet cells. Alginate gels enable the diffusion of nutrients and oxygen to the cells and the diffusion of insulin and metabolites out of the gel. Small spheres (≤0.5 mm) are engulfed in a layer of scar tissue (red) resulting from the action of macrophages and fibroblasts, drastically diminishing the lifetime of the islet cells. Larger spheres (≥1.5 mm) largely escape this foreign body reaction[3].

the occurrence of the three investigated macrophage subtypes (regulatory, pro-inflammatory and pro-healing): whereas all three subtypes were found on or near 0.5-mm spheres, regulatory macrophages were not found around the 1.5-mm implants (this is counterintuitive, as regulatory macrophages are known to play a role in the resolution of fibrosis[5,6]). Further observations will however be necessary to explain why the recruitment of macrophages (and subsequently myofibroblasts) is hampered.

The abrogation of the FBR by the larger spheres opens the door to improved biomedical applications. For example, extending the lifetime of transplanted islet cells should greatly facilitate the treatment of diabetic patients. Islets are typically encapsulated in semipermeable alginate spheres to protect the cells from rejection by the host and eliminate the need for immunosuppression[7]. However, due to the macrophage-mediated FBR (in particular, cellular overgrowth and deposition of a fibrotic matrix on the spheres), these implants ultimately fail. Traditional wisdom dictated the use of spheres smaller than 0.5 mm, as it was believed that this facilitates the diffusion of nutrients and oxygen to the cells. However, Anderson and co-authors' kinetic measurements of insulin and glucose diffusion within 0.5-mm and 1.5-mm alginate spheres demonstrates that there are no differences and that because the larger spheres abrogate the FBR, islet-loaded spheres of 1.5 mm allow for glucose levels in blood to be controlled for much longer (a greater than 5-fold prolonged duration).

Moreover, because the resistance to fibrosis is independent of the type of material and implantation site, the functional longevity of spherical implants for a variety of therapeutic modalities could be enhanced by simply making them larger. Furthermore, organ fibrosis — one of the most frequent causes of death in the Western world[8], with currently no treatments available — could be studied by implanting spheres of different diameters loaded with drugs with anti-fibrotic potential in separate subcutaneous pockets in a single animal, and then by monitoring the *in vivo* process in real time[9]. This should aid in the design of new therapeutics and in a reduction of the number of laboratory animals. ❐

*Ruud A. Bank is in the Department of Pathology and Medical Biology, University Medical Center Groningen, University of Groningen, 9713 GZ Groningen, The Netherlands.*
*e-mail: R.A.Bank@umcg.nl*

References
1. Anderson, J. M. & McNalley, A. K. *Semin. Immunopathol.* **33,** 221–233 (2011).
2. Londono, R. & Badylak, S. F. *Ann. Biomed. Eng.* **43,** 577–592 (2014).
3. Veiseh, O. *et al. Nature Mater.* **14,** 643–651 (2015).
4. Burnett, S. H. *et al. J. Leukoc. Biol.* **75,** 612–623 (2004).
5. Duffield, J. S. *et al. Annu. Rev. Pathol. Mech. Dis.* **8,** 241–276 (2013).
6. Lichtnekert, J. *et al. Curr. Opin. Pharmacol.* **13,** 555–564 (2013).
7. Scharp, D. W. & Marchetti, P. *Adv. Drug Del. Rev.* **67–68,** 35–73 (2014).
8. Wynn, T. A. & Ramalingam, T. R. *Nature Med.* **18,** 1028–1040 (2012).
9. Dang, T. T. *et al. Biomaterials* **32,** 4464–4470 (2011).

Published online: 18 May 2015

PHOTOVOLTAICS

# Perovskite cells charge forward

Now that certified energy conversion efficiencies for perovskite solar cells are above 20%, researchers are exploring other critical areas, such as understanding device hysteresis and film growth, as well as the replacement of lead and the development of tandem cell stacks. Cell stability remains a crucial issue.

Martin A. Green and Thomas Bein

Over the past few years, a new photovoltaic contender has emerged in the form of solar cells based on organic–inorganic lead halide perovskites[1], and, in particular, on methylammonium lead iodide ($MAPbI_3$). In November 2014, these perovskites joined the selected cohort of materials demonstrating a certified solar energy conversion efficiency above 20%. This demonstration was only 7 months after an efficiency of 18% was reported, affirming the technology's meteoric rise. As a comparison, a similar performance increase was realized in 14 months for CdTe cells, in 2 years for silicon (which has over 90% market share at present) and in 9 years for copper indium gallium selenide (CIGS) technology. Although this rapid progress