Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Biotechnology

# Editorial Overview: Nanotechnology and biotechnology: Two way traffic

Benjamin G Davis and Christopher J Serpell

**Current Opinion in Biotechnology** 2017, **46**:vi–viii

For a complete overview see the Issue

Available online 27th June 2017

http://dx.doi.org/10.1016/j.copbio.2017.06.002

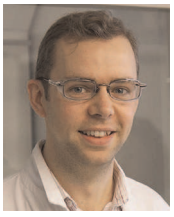


## Benjamin G Davis

Chemical Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK

Benjamin G Davis received his B.A. (1993) and D.Phil. (1996) at Oxford where he studied carbohydrates with George Fleet. After formative periods at the Universities of Toronto and Durham, he moved to Oxford in 2001 and was promoted to Professor in 2005. His research centres on the chemical understanding and exploitation of biomolecular function with an emphasis on carbohydrates and proteins. He is Editor-in-Chief of Current Opinion in Chemical Biology and a Senior Editor for ACS Central Science (2014). In 2015 he was elected to the Royal Society.

## Christopher J Serpell



School of Physical Sciences, University of Kent, Ingram Building, Canterbury, Kent CT2 7NH, UK
e-mail: c.j.serpell@kent.ac.uk

Chris Serpell is a Lecturer in Chemistry at the University of Kent. He obtained his MChem and DPhil at the University of Oxford with Paul Beer, before postdoctoral stints at

Over the past decades there has been a tremendous blossoming in both biotechnology and nanoscience. These advances have come through progress in techniques and instrumentation, step-changes in understanding, as well as the hard graft of innumerable scientists (thanks especially to the rapid growth outside of the US and Europe).

A common foundation for the two fields has been (and indeed one could argue must be) recognised: biology (protein, DNA, and lipid assemblies) transmits its functional effects on the nanoscale. This seemingly semantic point is more than that; the glib comment that 'Chemistry is nanotechnology' misses an essential distinction that the distances, levers, forces and transformations (including those that may drive bond manipulation) accomplished in biology are the product of effects transmitted over distance scales significantly larger than those found in small molecule transition states. This distinction is strategically important in considering how we interrogate the Chemistry of Biology; nanotechnology in this regard can be considered to be a 'size-matched' tool. Nonetheless, Chemistry acts as a shared language and provides a lens through which to understand core principles and tools to create new systems. New and interesting effects should therefore be expected to arise from the interaction of anthropogenic nanotechnology with Biology, whether through influence of nanomaterials on living systems, or by harnessing nature's nanoscale factories to fabricate our own designs. Fruitful crossover is also to be expected (and now increasingly observed) from use of shared analytical techniques. Nonetheless, the interface between the two fields is even less well understood than each individual area. Moreover, as both nanotech and biotech edge towards maturity, there is increasing pressure to deliver real-life applications. These impulses bring in the expertise of engineers and medical practitioners, further expanding the interdisciplinarity.

While there can be no doubt that there is enormous promise, there has at the same time also been a proliferation of fashions, buzzwords, and hype. Sometimes it has perhaps been all too tempting to use 'nano-something' to increase the profile of a bioscience paper, and *vice versa*. How much of this is useful? Our view is that the most transformational and translational technologies will emerge when nanotechnology brings some aspect of complete novelty to biology, or vice versa, leading to something greater than the sum of the parts [1]. Fittingly, 'greater than the sum of its parts' could be said to be the trait most strikingly manifest in living systems, which achieve outcomes well beyond our technological capability on the basis of simple molecular building blocks assembled through the functional filter of fitness; the resulting complexity solves problems that are typically beyond

McGill University (with Hanadi Sleiman), and again at Oxford (with Ben Davis). His work revolves around the creation of self-assembled nanoscale constructs based on sequenced polymers and supramolecular chemistry to solve problems in biology.

the reach of any blockwise, homogeneous design. In this Special Issue, we have chosen to highlight specifically the '*two-way traffic*' between these disciplines — we have aimed to highlight examples of unique possibilities being raised in bio-technology or nano-technology through contribution of the other.

## Using biotechnology to advance nanoscience

In the first set of examples, biology provides tools to create nanostructures which would be otherwise inaccessible. The diversity of natural peptides is both a strength and challenge for nanotechnology. Slocik and Naik [2] lay out how sequenced biomolecules like peptides and oligonucleotides can lead to highly selective binders for nanomaterials, and act as adjuncts to control size and shape. Improvements in methods for selection and sequencing through phage display are documented, as are applications as diverse as strengthening steel and adherence of hair dye. At the next scale up, Voet and Tame document the ability of full proteins to template inorganic nanoparticles [3]. Starting with more obvious cage-type proteins (ferritin, viruses), the review moves to less intuitive, but readily available templates like bovine serum albumin and lysozyme to generate nanoparticles and nanowires. The discussion moves on to a particularly impressive achievement — the templation of the smallest mineral crystal yet characterised structurally. Kobayashi and Arai set out the latest developments in design of nanostructures using proteins themselves as building blocks [4]. While DNA nanotechnology has succeeded because of its simplicity, the very sophistication of proteins has made it much more difficult to create programmed non-natural nanostructures. However, some design rules for production of artificial protein structures are now being elucidated using the fusion of self-assembling protein domains.

## Using nanoscience to advance biotechnology

The second set of reviews explore the use of nanotechnological methods to solve problems in biotechnology. Membrane proteins are key players in cellular processes, providing contact with the outside world, yet their full characterisation remains a challenge. Their native folding and function requires membrane incorporation, yet lipid systems are sensitive and temperamental. Hu et al. discuss the use of synthetic polymersome systems as hosts for analysis of membrane proteins [5]. Polymersomes are potent tools, providing both robustness and customisability, and can be integrated with cell-free protein synthesis. Stem cells, another promising technology, have the potential to revolutionise regenerational medicine but control of their differentiation into functional tissues is still poorly understood. The vast parameter space available in choice of environmental conditions which can lead to the formation of one type of cell rather than another is a significant challenge. Tronser et al. discuss the miniaturisation of high-throughput arrays designed to discover these conditions [6]. Both the construction of high-density arrays, and the creation of specific environments akin to the extracellular matrix are examined. Another problem in biotechnology is the phenomenon of the protein corona. Nanomaterials in biological fluids tend to adsorb various proteins, creating an external shell. Since this covering will necessarily affect the chemical and physical properties of the particles, knowledge of its extent and nature are essential for successful deployment of nanobiotechnologies. Carrillo-Carrion et al. expound the techniques available to answer this question [7]. The field is divided into 'direct' methods which probe the protein layer itself and can identify its composition, and 'indirect' methods which rely on gross changes to infer details of the protein corona.

## Mimicking, exploiting, and influencing biological processes with nanotechnology

Next, we go beyond structural studies to look at the interface of nanotechnology with biological processes. One characteristic of living systems is that they operate far from equilibrium — there is a constant need for inputs and outputs to drive processes energetically uphill; the translation of this principle into nanotechnology is outlined by della Sala et al. [8]. By tethering nanoscale self-assembly to chemical oscillations, it is possible to mimic Biology in terms of control over structure in the temporal domain. Examples of this include cycling gelators, and transient vesicular systems. DelRosso and Derr then take us through nature's conveyor belts — cytoskeletal transport mechanisms [9]. These are the gold standard of nanoscale transport — directional, long range, and efficient. Efforts to exploit and mimic these systems for controlled delivery of non-natural cargo are explored, and purely synthetic examples of genuine nanoscale walking machines showcased. Conversely, Giessen and Silver discuss efforts towards using nanotechnology to improve biological processes, photosynthesis in this case [10]. Carbon fixation is a growing problem and current crops are poorly optimised to tackle it; the review shows how engineering of chloroplasts to ensure the most efficient conversion of carbonate into sugars can yield potentially game-changing new technologies.

## Nanobiotechnology in the field

Our final block of perspectives looks at how nanobiotechnologies bring something new to real life settings. Scheinberg et al. assess the progress that nanotechnology has made in the clinic [11]. Highlighting the general benefits of multivalency and multifunctionality that nanomaterials display, the still poorly understood pharmacology is reviewed. Outstanding examples in the fields of imaging, therapeutics (including non-liposomal cases), and external sensors are presented, and the hurdles and opportunities ahead scoped out. Strauss and Chmielewski take a closer look at one case — the use of self-assembling collagen mimetic peptides to create customisable matrices for tissue regeneration [12]. The strategies needed to generate assemblies from the molecular level, through the nanoscale, to macroscopic materials are presented, followed by exciting results on the growth of cells in the matrices. As well as the anticipated benefits, nanotechnology can also bring unexpected novelties. For industries in nanotechnology, the risk of causing harm to humans or the ecosystems must be managed, while still leaving room for innovation to flourish. Auty addresses these questions through the lens of risk appetite [13]. The toxicological risks associated with nanotechnologies are reviewed, and a control banding scheme proposed as a way to manage such aspects of these highly promising materials. Lastly, the final destination and effects of nanomaterials in the ecosystem is clearly an important area of concern, as the number of nanoparticle-containing products rapidly increases. Mottier et al. look at the risk posed by such xenobiotic materials in the environment [14]. Taking carbon nanomaterials as a case study, the difficulties of detection, and questions of aging and transformation are discussed. The effects of carbon nanomaterials on amphibians and photosynthetic microorganisms have been determined experimentally, and the significance of these findings is highlighted. This perspective serves as a valuable signpost for future management of nanomaterials in the ecosystem.

We hope that this collection of perspectives will showcase what is genuinely new and exciting at the interface of nanotechnology and biotechnology, and inspire readers to move forward to conceive new possibilities and applications that fully exploit the common foundations of the two areas.

## References


1. Serpell CJ, Kostarelos K, Davis BG: **Can carbon nanotubes deliver on their promise in biology? Harnessing unique properties for unparalleled applications**. *ACS Cent Sci* 2016, **2 (4)**:190-200.
2. Slocik JM, Naik RR: **Sequenced defined biomolecules for nanomaterial synthesis. Functionalization, and assembly**. *Curr Opin Biotechnol* 2017, **46**:7-13.
3. Voet AR, Tame JR: **Protein-templated synthesis of metal-based nanomaterials**. *Curr Opin Biotechnol* 2017, **46**:14-19.
4. Kobayashi N, Arai R: **Design and construction of self-assembling supramolecular protein complexes using artificial and fusion proteins as nanoscale building blocks**. *Curr Opin Biotechnol* 2017, **46**:57-65.
5. Hu Z, Ho JCS, Nallani M: **Synthetic (polymer) biology (membrane): functionalization of polymer scaffolds for membrane proteins**. *Curr Opin Biotechnol* 2017, **46**:51-56.
6. Tronser T, Popova AA, Levkin PA: **Miniaturized platform for high-throughput screening of stem cells**. *Curr Opin Biotechnol* 2017, **46**:141-149.
7. Carrillo-Carrion C, Carril M, Parak WJ: **Techniques for the experimental investigation of the protein corona**. *Curr Opin Biotechnol* 2017, **46**:106-113.
8. della Sala F, Neri S, Maiti S, Chen JL-Y, Prins LJ: **Transient self-assembly of molecular nanostructures driven by chemical fuels**. *Curr Opin Biotechnol* 2017, **46**:27-33.
9. DelRosso NV, Derr ND: **Exploiting molecular motors as nanomachines: the mechanisms of de novo and re-engineered cytoskeletal motors**. *Curr Opin Biotechnol* 2017, **46**:20-26.
10. Giessen TW, Silver PA: **Engineering carbon fixation with artificial protein organelles**. *Curr Opin Biotechnol* 2017, **46**:42-50.
11. Scheinberg DA, Grimm J, Heller DA, Stater EP, Bradbury M, McDevitt MR: **Advances in the clinical translation of nanotechnology**. *Curr Opin Biotechnol* 2017, **46**:66-73.
12. Strauss K, Chmielewski J: **Advances in the design and higher-order assembly of collagen mimetic peptides for regenerative medicine**. *Curr Opin Biotechnol* 2017, **46**:34-41.
13. Auty AR: **Quantifying environmental and personal risks of nanotechnology for industry**. *Curr Opin Biotechnol* 2017, **46**:150-155.
14. Mottier A, Mouchet F, Pinelli É, Gauthier L, Flahaut E: **Environmental impact of engineered carbon nanoparticles: from releases to effects on the aquatic biota**. *Curr Opin Biotechnol* 2017, **46**:1-6.