Exploring the potential of metallic nanoparticles within synthetic biology

ELSEVIER

Exploring the potential of metallic nanoparticles within synthetic biology

Research Paper

Matthew C. Edmundson, Michael Capeness and Louise Horsfall

School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3JR, UK

The fields of metallic nanoparticle study and synthetic biology have a great deal to offer one another. Metallic nanoparticles as a class of material have many useful properties. Their small size allows for more points of contact than would be the case with a similar bulk compound, making nanoparticles excellent candidates for catalysts or for when increased levels of binding are required. Some nanoparticles have unique optical qualities, making them well suited as sensors, while others display para-magnetism, useful in medical imaging, especially by magnetic resonance imaging (MRI). Many of these metallic nanoparticles could be used in creating tools for synthetic biology, and conversely the use of synthetic biology could itself be utilised to create nanoparticle tools. Examples given here include the potential use of quantum dots (QDs) and gold nanoparticles as sensing mechanisms in synthetic biology, and the use of synthetic biology to create nanoparticle-sensing devices based on current methods of detecting metals and metalloids such as arsenate. There are a number of organisms which are able to produce a range of metallic nanoparticles naturally, such as species of the fungus *Phoma* which produces anti-microbial silver nanoparticles. The biological synthesis of nanoparticles may have many advantages over their more traditional industrial synthesis. If the proteins involved in biological nanoparticle synthesis can be put into a suitable bacterial chassis then they might be manipulated and the pathways engineered in order to produce more valuable nanoparticles.

Introduction

The study of the creation and application of nanoparticles forms an up-and-coming branch of materials science. Typically defined as being a material on the nano-scale (anywhere from 1 to 100 nm in one of their dimensions [1]), we are employing nanoparticles in an ever increasing number of applications in medicine and industry [2,3], and as new tools to aid fundamental scientific research [4]. Nanoparticle properties are very diverse. The properties of the core molecule used, what modifications and functionalisations are made, their size and shape, and any secondary or tertiary structures the nanoparticles are able to form all give rise to the multitude of useful properties nanoparticles exhibit. Their small surface area to volume ratios make them ideal for use as catalysts [5] and the crystal structures some nanoparticles form have unique optical properties [6]. There are many different types of nanoparticles, from lipid-based vesicles for drug delivery to the carbon nanotube, but one of the more diverse and wide-spread types is the metallic nanoparticle. This review will give a brief outline of metal nanoparticles, before looking at how the fields of metallic nanoparticle research and synthetic biology could come together with huge benefits to both.

Metallic nanoparticles

Many metal and metalloid elements are able to form nano-scale structures. Some of the better known nanoparticles currently being investigated include those based on silver, which are known for their anti-microbial and anti-inflammatory properties [7]. Silver has long been known for its ability to combat infection [8], being able to inhibit various aspects of respiration; silver nanoparticles have

Corresponding authors: Edmundson, M.C. (medmunds@staffmail.ed.ac.uk), Horsfall, L. (louise.horsfall@ed.ac.uk)

1871-6784/$ - see front matter © 2014 Published by Elsevier B.V. http://dx.doi.org/10.1016/j.nbt.2014.03.004

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

TABLE 1

Summary of the metallic nanoparticles produced by various prokaryotic (A) and eukaryotic (B) organisms

Bacterial strain	Metal nanoparticles produced
A	
Desulfovibrio sp.	Au, Cr, Pd, Pt
Magnetospirillum gryphiswaldense	Fe
Shewanella sp.	Fe
Cupriavidus metallidurans	Cd, Cu, Co, Ge, Ni, Pb, Pd, Y, Zn
Pseudomonas sp.	Ag, Co, Fe, Li, Ni, Pd, Pt, Rh, Ru
Organism	**Metal nanoparticles produced**
B	
Phoma sp.	Ag
Fusarium oxysporum	Ag, Au, Cd, Pb, Pt, Ti, Zr
Rhizophora mucronata	Ag

larger surface areas, increasing the area available for interactions, making them even more effective anti-microbial agents [9]. Gold nanoparticles are being utilised in imaging, with colloidal gold nanoparticles used in the immunogold labelling of samples to be viewed using transmission electron microscopy (TEM) [10]. The gold nanoparticles are conjugated to a secondary antibody able to bind to a primary antibody, which in turn is raised against a specific target. The electron-dense gold nanoparticles show up as dark spots, allowing the target to be visualised. Also used in imaging are magnetic nanoparticles as contrast agents in magnetic resonance imaging (MRI) scans. There is a wide range of para-magnetic metal nanoparticles, mostly but not exclusively based on iron. When an external magnetic field is applied these nanoparticles become magnetic themselves, and align themselves with the direction of the external field, showing up as a hypo-exposed region on an MRI scan [11]. Iron-based magnetic nanoparticles, such as Feridex, have mostly been used *in vitro* or *in vivo* in experiments, for example in tracking the movement of stem cells implanted into a wound site [12,13]. Nanoparticles are also being put to use in the treatment of diseases. Gold nanoparticles are being used as drug delivery systems [14,15], and some nanoparticles have disease-countering intrinsic properties. Iron-based nanoparticles have been targeted specifically to cancer cells via mesenchymal stem cells able to home in on sites of tumorgenesis; when an external magnetic field is applied the nanoparticles heat up, killing the cancer cells via thermal damage [16]. Catalytic metallic nanoparticles have been developed for a wide array of reactions, from palladium nanoparticles performing Suzuki reactions in the production of styrenes [17] to oxygen reduction reactions in fuel cells performed by platinum nanoparticles [18]. The current boom in these nanoparticle catalysts is seeing extensive research carried out in the design, production and optimisation of these catalysts [19]. Metal nanoparticles also have applications in electronics, photonics and in environmental clean-up, amongst others. Clearly they are a class of material with huge potential.

Metallic nanoparticles and synthetic biology

Synthetic biology involves the re-engineering of life to create organisms capable of performing novel functions for industry, medicine and scientific research. Synthetic biology could be enriched by exploring the possibilities metallic nanoparticles provide, and the same is true vice versa; synthetic biology has the potential to be a powerful tool in the production and functionalisation of metal nanoparticles. The modular nature of synthetic biology lends itself very well to metal nanoparticle production. With the ability to swap modules in and out of a chassis it would allow the production of nanoparticles based on many different elements as well as a large number of post-production modifications to a core nanoparticle. By treating the nanoparticles as modular many useful materials can be produced. One area in which it makes sense to begin this joint effort is sensing, both in using nanoparticles as sensors in synthetic biology applications and in using synthetic biology to create methods of sensing the nanoparticles themselves. Once reliable sensing methods have been developed they can form the foundation for producing nanoparticles with other properties, such as catalysts or conductive nanowires.

In creating metallic nanoparticle-based tools for synthetic biology a good starting point would be quantum dots (QDs). QDs are a class of nanocrystals that emit light of specific wavelengths with the size of the nanoparticle determining the wavelength; the larger the size, the higher the wavelength of the infra-red light emitted [20]. A potential hazard in binding QDs to a protein of interest is the fact that QDs can be multivalent. While it is relatively straight forward to bind QDs to proteins, they are capable of additional interactions with the protein and may affect its function. To avoid this complication a method has been developed using phosphorothioate DNA (ptDNA) to 'wrap around' commercially available CdSe:ZnS QDs, blocking all other potential binding sites (Fig. 1). The ptDNA can be further modified, such as by conjugation with benzylguanine, a molecule which binds SNAP tags. This method was successfully used to target ptDNA/QD particles to Notch receptors carrying a SNAP tag; as CdSe:ZnS QDs emit light at 605 nm the location of these Notch receptors in the cells could then be determined using an imaging microscope and a 488 nm laser [21]. Such a sensing method could readily be applied to any protein of interest. In synthetic biology it is often important to determine the location of a protein of interest, such as ensuring a protein of interest with a trans-membrane domain has been successfully inserted into the membrane. The use of QDs in the manner described would therefore be very useful.

Similarly it is possible to use metal nanoparticles to detect single proteins *in situ* in mammalian cells. 10 nm gold nanoparticles have been produced which absorb a particular wavelength of lased light. This absorption leads to a temperature change, changing the refractive properties of the nanoparticle, which is detected using a second laser. This method was successfully used to detect the gold nanoparticle labelled-protein mGluR5 (a neurotransmitter-receptor protein) within the cell membrane [22]. This method is a less intrusive way of investigating the trafficking of individual proteins compared to conjugating bulky fluorescence proteins to the protein of interest.

There are also examples of synthetic biology projects with the potential to act as sensors for metal nanoparticles. Synthetic biology is already being used to create ways of sensing elemental and molecular forms of metals, and it is easy to see how these could be modified and expanded upon to create ways of sensing metallic nanoparticles. With the biological production of metal nanoparticles becoming more widespread such sensors would be useful in a

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

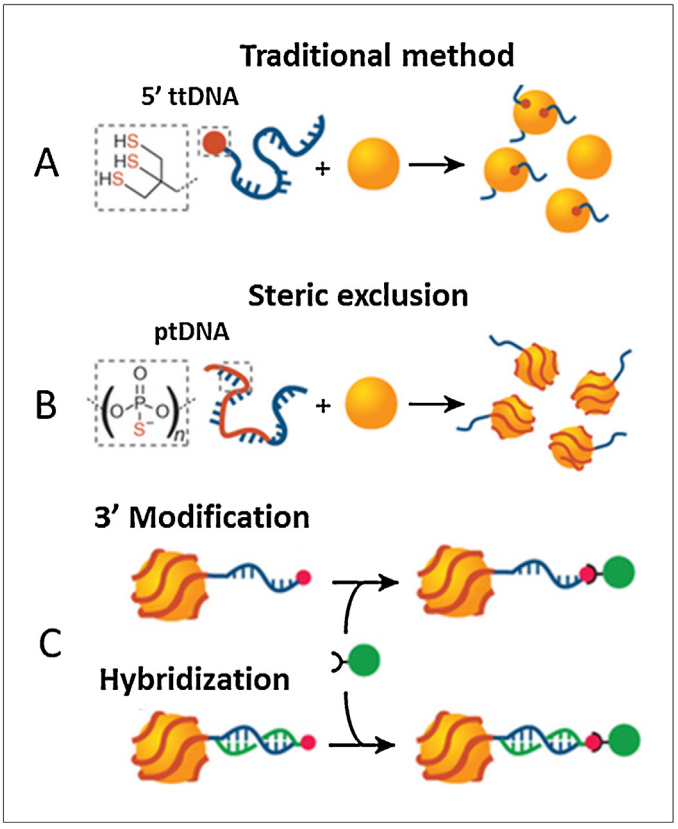

FIGURE 1

Linking materials to quantum dots. **(a)** Traditional method. Trithiolated DNA (ttDNA) binding to quantum dots (gold spheres) yields multivalent and non-conjugated products, as well as desired monovalent products. **(b)** Steric exclusion method. Phosphorothioate DNA (ptDNA) is able to wrap around the quantum dots, forming only monovalent products. **(c)** Subsequent 3′ modification of the 3′ end of the ptDNA allows the conjugation of the quantum dots to the desired target [21].

detection system which gives a visual indication (e.g. by GFP) when a certain concentration of nanoparticles has been produced, or as part of a feedback mechanism to turn off genes involved in nanoparticle production. Additionally these sensors could have a role to play in the traditional synthesis of metal nanoparticles. It is possible to engineer high specificity in biological detection systems, allowing the purity of the synthesised nanoparticles to be assessed. One example of a metalloid-sensing system that could be used as starting point in engineering nanoparticle-detecting systems uses *Escherichia coli* to sense the presence of arsenite [23]. The sensing is achieved by combining short-range quorum sensing between cells within individual colonies on the sub-mm scale with an amplification system which depends on the longer range release and detection of gaseous metabolites on the mm scale between different colonies. Individual cells sensing arsenite communicate this to nearby cells in the colony. This synchronised colony is then able to send out an alternative and stronger signal to nearby colonies, bringing the reporter mechanism above the detection threshold. The 'nesting' of communication described here allows any background activity caused by used fluctuations in the quorum signalling of a single colony to be overcome, preventing false positives. The DNA constructs encoding the sensing machinery include several different elements, including: an arsenite-responsive promoter, the *luxR* gene, and a signal oscillation/reporter element (Fig. 2). This robust and highly tuned sensing pathway with designed modularity could easily be adapted to include any other substrate, such as a metallic nanoparticle, and as such has wide applications.

Salmonella enterica is able to detect Fe(III) via the membrane protein PmrB [24]. When extracellular levels of iron are high, PmrB auto-phosphorylates, and is then able to activate PmrA. This in turn interacts with the promoters of genes involved in iron metabolism and transport [24]. Work has been carried out to replace the iron-sensing domain of PmrB with other metal-binding domains; as there are no known wild type proteins capable of binding to lanthanide group metals, artificial lanthanide-binding peptides [25] have been used to replace the iron-binding domain in PmrB in an *E. coli* chassis [26]. This strain also contains PmrA, as well as a reporter gene such as GFP under the control of a PmrA-controlled promoter. Thus when PmrB detects a lanthanide it is specific to it activates PmrA, which in turn drives the production of the reporter protein [26]. These are just two examples of how synthetic biology has been put to use in the sensing of metal substrates, and from being able to sense metal substrates it is relatively easy to engineer systems to sense nanoparticles of those metals. These systems would constitute a powerful tool in synthetic biology, and produce a very customisable system for the detection many substrates, including metal nanoparticles.

Bacterial/biological production of metal nanoparticles

As well as advances in sensing, synthetic biology offers new approaches in the synthesis and modification of biological nanoparticles. While metallic nanoparticles are widely used in many applications the current chemical and physical methods for their synthesis can be problematic, often requiring high temperatures and/or pressures, making them very energy intensive processes and therefore expensive [27]. Additionally, the starting materials for these methods can be expensive and often require very pure grades of substrate. Biological synthesis, however, offers a number of benefits over synthetic processes for nanoparticle production, including: lower reaction temperatures, lower working pressures, the use of a non-pure starting material and cheaper maintenance of the 'catalyst' [27,28]. As such, there has been a lot of research carried out using both prokaryotic and eukaryotic organisms to produce metallic nanoparticles with some attributed applications. Organisms generally make nanoparticles as part of their defence against toxic metals. These organisms lower the toxicity of metal ions by reducing them to elemental or less toxic/soluble forms as a by-product of ATP synthesis, and often transport them outside of the cell [29,30].

Both eukaryotes and prokaryotes are known to produce and implement nanoparticles; a summary of the organisms covered in this review and the types of nanoparticle they produce are given in Table 1. One example of a eukaryotic nanoparticle producer is the fungus *Phoma*, which produces silver nanoparticles as antibacterial agents, and these have been found to have uses as catalysts in the oil industry and for medical applications [27]. *Fusarium oxysporum* produces nanoparticles of Pt, Zr, Ag, Au, Cd, Pb and Ti [31–33], and the mangrove plant *Rhizophora mucronata* has been shown to produce antimicrobial silver nanoparticles [34].

However, due to their faster growth rates and ease of manipulation, nanoparticle-producing prokaryotes are the logical choice for developing nanoparticles in synthetic biology, especially since

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

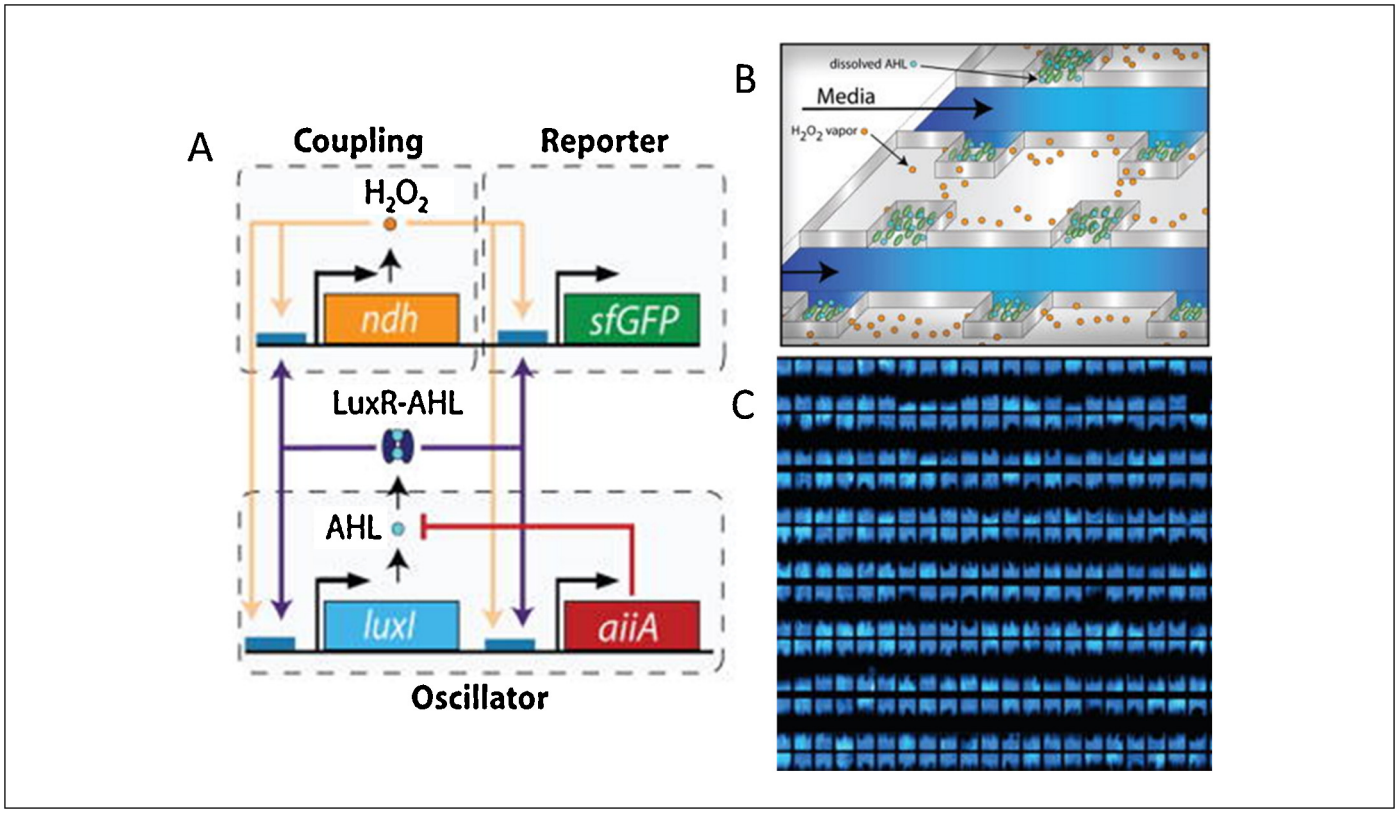

FIGURE 2

Arsenic sensing system. **(a)** Schematic of the arsenite sensing construct. All of the genes are driven by a *luxI* promoter. The LuxI protein produces AHL which forms a complex with LuxR; this drives expression from the *luxI* promoters in cells within the same colony, synchronising them. *ndh* encodes NDH-2, an enzyme that generates H_2O_2 vapour; this diffuses to nearby colonies and activates the system there, synchronising them to the original colony. **(b)** Overview of colonies. AHL diffuses intra-colonially, synchronising single colonies; H_2O_2 vapour diffuses inter-colonially, synchronising adjacent colonies. **(c)** Fluorescence produced by synchronised colonies. Each square is one colony made up of approximately 500 cells [23].

many species of bacteria are able to produce nanoparticles naturally. Sulphur reducing bacteria, such as *Desulfovibrio*, can reduce certain metals such as Au, Pt and Pd to nanoparticle forms. Palladium nanoparticles produced by *Desulfovibrio* have been shown to be an effective catalyst in hydrogen fuel cells [35] while palladised *Desulfovibrio* cells have also been used in chromium (IV) decontamination. These nanoparticles proved to be very stable, lasting over eleven times longer than industrially produced palladium nanoparticles [36].

A bacterium that utilises nanoparticles internally is *Magnetospirillum gryphiswaldense*, which produces magnetic nanoparticles. These aquatic magnetotactic bacteria produce magnetic nanocrystals and encase them in membranes [37], forming structures known as magnetosomes (Fig. 3) possibly for orientation and chemotaxis purposes [38]. This offers the possibility of producing 'pre-packaged' nanoparticles.

As well as structures like the magnetosome, a form of nanoparticle known as a nanowire is also produced naturally by some organisms. In respiration under anaerobic conditions *Shewanella* are able to transport electrons out of the cell along metal nanowires [39] (Fig. 4). The nanowires increase the surface area available to the cell to 'discharge' electrons, increasing the rate of electron transfer during respiration. As well as being investigated for their potentially useful conductive properties the compounds produced by the reduction carried out by the nanowires are also worth exploring. Of note is the fact that *Shewanella* produce nanowires that are able to reduce silica ferrihydrite to magnetite (Fe_3O_4) nanoparticles [39]; these have paramagnetic properties, and as mentioned above are used as contrast agents in MRI [11].

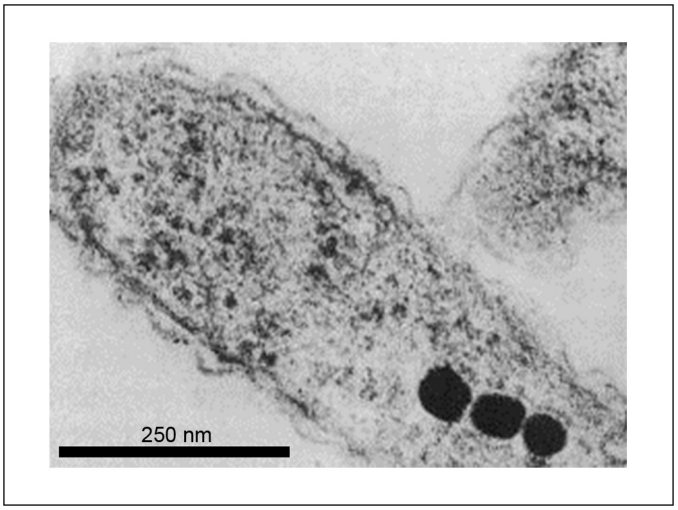

FIGURE 3

Bacteria containing magnetosomes (black circular structures) composed of iron nanoparticles. Thin sections of sample were stained with 5% uranyl acetate and 0.4% lead citrate, and imaged using TEM. Scale bar: 250 nm [37].

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

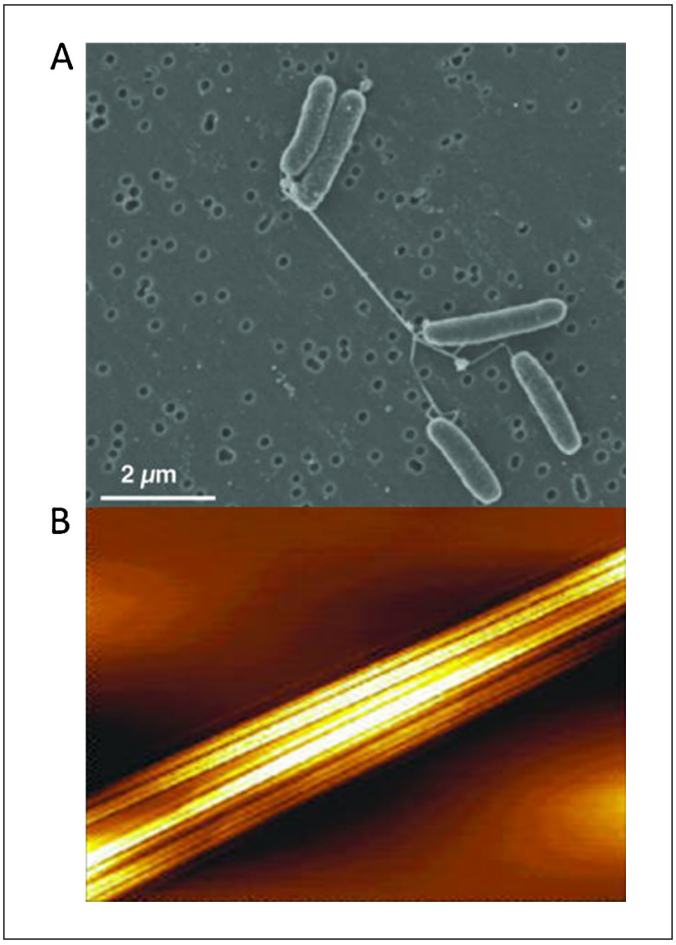

FIGURE 4

Bacterial nanowires. **(a)** Scanning electron microscopy image of *Shewanella oneidensis* producing nanowires. **(b)** Scanning tunnelling microscope image of nanowire conducting electric current [39].

Some bacteria capable of reducing metals to nanoparticle forms have been used in industrial applications. One such bacterium highlighted in early work by Diels [40] is *Cupriavidus metallidurans* (previously *Alcaligenes eutrophus*). It was shown that it could reduce the metals Cd, Cu, Zn, Co, Ni, Pb, Pd, Y and Ge, when they were present as soil contaminants at former industrial sites, precipitating them in carbonate forms that could be removed more easily. This work points out how value can be added to the use of bacteria as a remediation strategy; not only were the organisms used to treat contaminated land but in future they might also be used to retrieve metals for future use. It also showed that the use of non-pure substrates, in this case soil, is also a possibility and puts to work the bacteria's highly selective 'sieve-like' nature to absorb those useful metals and reduce them, often into pure elemental forms of nanoparticle.

Another bacterium of potential industrial value is *Pseudomonas*, which has recently been shown to produce a large array of nanoparticles; work by Srivastava [41] found that *Pseudomonas* produced nanoparticles of Ag, Pd, Fe, Rh, Ni, Ru, Pt and Co, and surprisingly Li as well. All of the nanoparticles were produced at room temperature (Fig. 5), highlighting how little energy is required for their synthesis compared to current methods [41].

Cupriavidus and *Pseudomonas* together are able to produce a large number of highly desirable metals in their wild-type forms; it is easy to see how synthetic biology could be used to take such diversity as a starting point and engineer bacteria for wider applications, such as contaminant identification/detoxification as well as the specific production of a nanoparticle from a mixture of substrates such as found in soil or water.

Possible limitations

As with most advancements in science and technology there are potential drawbacks and controversial issues. Synthetic biology is certainly no different; the end products are designed to be used in real-life applications, often in areas where they have contact with people outside of science, either in industry or medicine, and as such is at the forefront of public debate. Additionally nanoparticles are a relatively new class of material with characteristics quite different to those of larger scale samples of the same material, where even small differences in size lead to different catalytic properties. Therefore, especially in medicine, the use of nanoparticles is somewhat controversial. Quantum dots have uses in medical research and diagnosis, but in other studies were found to be toxic to cells *in vivo*, leading to an apparent discrepancy between applications and implementations [42].

The problems with using nanoparticles are that for each reported use they have different characteristics, different derivation or are being used in quite different systems, and very little is yet known about their impact on the environment or in potential patients [43]. The solution to this would be standardisation of the nanoparticles used; this is something that is integral to synthetic biology, as standardisation is fundamental to implementation and ease of use. One illustrative example of how standardisation has been implemented is in the form of Biobricks for bacterial genetic manipulation [44,45]. The Biobrick project consists of a large number of standard parts (such as genes and promoters) available to anyone and which can be readily combined into new constructs [46]. This engineering approach to synthetic biology offers a huge number of possible biobrick functions.

As well as drawbacks found with metal nanoparticles themselves there are also potential pitfalls with their biological production. Current methods will need to be optimised in order to ensure that the metal nanoparticles are all of the desired size and composition. It may also be necessary to first engineer a chassis so that it is able to survive in the presence of nanoparticles and their substrates as these may prove toxic to the cells; as mentioned above many of the natural pathways of nanoparticle synthesis in bacteria evolved to deal with the toxicity of metal-containing compounds [29]. Additionally for schemes such as bioremediation there is the issue of releasing engineered organisms into the environment. It would therefore be necessary to use separate strains, using wild-type organisms able to accumulate metals from contaminated land and only using engineered nanoparticle-forming organisms in a controlled environment.

It is the role of synthetic biology, as with all branches of science, to innovate responsibly and to take great care with the synthesis of new materials, and when synthetic biology-inspired standardisation methods and practices are implemented we can begin to assess and control the impact nanoparticles and their production have in applied systems and the environment.

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

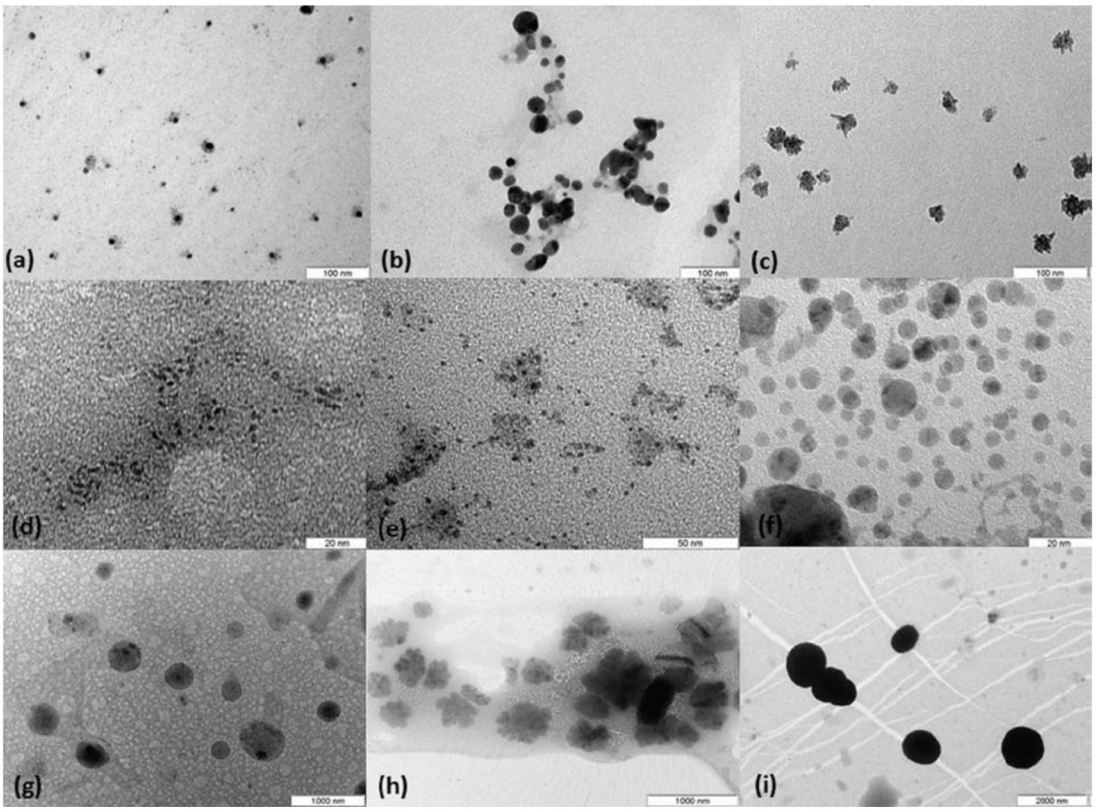

FIGURE 5

TEM image of the wide array of nanoparticles produced by *Pseudomonas aeruginosa* SM1[41]. **(a)** Ag, **(b)** Pd, **(c)** Fe, **(d)** Rh, **(e)** Ni, **(f)** Ru, **(g)** Pt, **(h)** Co, **(i)** Li.

Summary

This review has explored many of the possibilities offered by bringing together aspects of synthetic biology and metallic nanoparticles. Using metallic nanoparticle tools as part of synthetic biology, and using synthetic biology to produce and modify nanoparticles, both fields can achieve a great deal of synergy. Synthetic biology is about adapting existing natural biological capabilities to facilitate the solving of issues faced by science, engineering and medicine. There is a large array of metallic nanoparticle-forming pathways that already exist in nature, ready to be utilised by synthetic biology in producing 'natural' and synthetic nanoparticles that are able to compete with industrial products at commercial levels. Real-world applications, such as using synthetic biology to create bacteria capable of cleaning up former industrial sites and converting metal contaminants into useful nanoparticles, are already being investigated. Further work is needed, but unlocking the potential of combining metallic nanoparticles and synthetic biology is worth the effort.

References

[1] Zamborini FP, Bao L, Dasari R. Nanoparticles in measurement science. Anal Chem 2012;84(2):541–76.
[2] Schmid K, Riediker M. Use of nanoparticles in Swiss industry: a targeted survey. Environ Sci Technol 2008;42(7):2253–60.
[3] Loomba L, Scarabelli T. Metallic nanoparticles and their medicinal potential. Part II: Aluminosilicates, nanobiomagnets, quantum dots and cochleates. Ther Deliv 2013;4(9):1179–96.
[4] Kane AL, Bond DR, Gralnick JA. Electrochemical analysis of *Shewanella oneidensis* engineered to bind gold electrodes. ACS Synth Biol 2013;2(2):93–101.
[5] Wang P. Nanoscale biocatalyst systems. Curr Opin Biotechnol 2006;17(6):574–9.
[6] Radwan SH, Azzazy HM. Gold nanoparticles for molecular diagnostics. Expert Rev Mol Diagn 2009;9(5):511–24.
[7] Chaloupka K, Malam Y, Seifalian AM. Nanosilver as a new generation of nanoproduct in biomedical applications. Trends Biotechnol 2010;28(11):580–8.
[8] Chen X, Schluesener HJ. Nanosilver: a nanoproduct in medical application. Toxicol Lett 2008;176(1):1–12.
[9] Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv 2009;27(1):76–83.
[10] Mayhew TM, Muhlfeld C, Vanhecke D, Ochs M. A review of recent methods for efficiently quantifying immunogold and other nanoparticles using TEM sections through cells, tissues and organs. Ann Anat 2009;191(2):153–70.
[11] Edmundson M, Thanh NT, Song B. Nanoparticles based stem cell tracking in regenerative medicine. Theranostics 2013;3(8):573–82.
[12] Bulte JW, Zhang S, van Gelderen P, Herynek V, Jordan EK, Duncan ID, et al. Neurotransplantation of magnetically labeled oligodendrocyte progenitors: magnetic resonance tracking of cell migration and myelination. Proc Natl Acad Sci U S A 1999;96(26):15256–61.
[13] Okada T, Sasaki F, Kamiyama T, Nakagawa T, Nakanishi K, Kobayashi R, et al. Focal nodular hyperplasia of the liver: usefulness of superparamagnetic iron oxide-enhanced magnetic resonance imaging. J Pediatr Surg 2005;40(3):E21–5.
[14] Aili D, Gryko P, Sepulveda B, Dick JA, Kirby N, Heenan R, et al. Polypeptide folding-mediated tuning of the optical and structural properties of gold nanoparticle assemblies. Nano Lett 2011;11(12):5564–73.

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004

[15] Ghosh P, Han G, De M, Kim CK, Rotello VM. Gold nanoparticles in delivery applications. Adv Drug Deliv Rev 2008;60(11):1307–15.
[16] Ruan J, Ji J, Song H, Qian Q, Wang K, Wang C, et al. Fluorescent magnetic nanoparticle-labeled mesenchymal stem cells for targeted imaging and hyperthermia therapy of in vivo gastric cancer. Nanoscale Res Lett 2012;7(1):309.
[17] Li Y, Hong XM, Collard DM, El-Sayed MA. Suzuki cross-coupling reactions catalyzed by palladium nanoparticles in aqueous solution. Org Lett 2000;2(15):2385–8.
[18] Wei GF, Liu ZP. Optimum nanoparticles for electrocatalytic oxygen reduction: the size, shape and new design. Phys Chem Chem Phys 2013;15(42):18555–61.
[19] Chen P, Zhou X, Andoy NM, Han KS, Choudhary E, Zou N, et al. Spatiotemporal catalytic dynamics within single nanocatalysts revealed by single-molecule microscopy. Chem Soc Rev 2013;43:1107–17.
[20] Nath D, Banerjee P. Green nanotechnology – a new hope for medical biology. Environ Toxicol Pharmacol 2013;36(3):997–1014.
[21] Farlow J, Seo D, Broaders KE, Taylor MJ, Gartner ZJ, Jun YW. Formation of targeted monovalent quantum dots by steric exclusion. Nat Methods 2013;10(12):1203–5.
[22] Cognet L, Tardin C, Boyer D, Choquet D, Tamarat P, Lounis B. Single metallic nanoparticle imaging for protein detection in cells. Proc Natl Acad Sci U S A 2003;100(20):11350–55.
[23] Prindle A, Samayoa P, Razinkov I, Danino T, Tsimring LS, Hasty J. A sensing array of radically coupled genetic 'biopixels'. Nature 2012;481(7379):39–44.
[24] Wosten MM, Kox LF, Chamnongpol S, Soncini FC, Groisman EA. A signal transduction system that responds to extracellular iron. Cell 2000;103(1):113–25.
[25] Franz KJ, Nitz M, Imperiali B. Lanthanide-binding tags as versatile protein coexpression probes. Chembiochem 2003;4(4):265–71.
[26] Liang H, Deng X, Bosscher M, Ji Q, Jensen MP, He C. Engineering bacterial two-component system PmrA/PmrB to sense lanthanide ions. J Am Chem Soc 2013;135(6):2037–9.
[27] Chen JC, Lin ZH, Ma XX. Evidence of the production of silver nanoparticles via pretreatment of *Phoma* sp.3.2883 with silver nitrate. Lett Appl Microbiol 2003;37(2):105–8.
[28] Faramarzi MA, Sadighi A. Insights into biogenic and chemical production of inorganic nanomaterials and nanostructures. Adv Colloid Interface Sci 2013;189–190:1–20.
[29] Hennebel T, De Gusseme B, Boon N, Verstraete W. Biogenic metals in advanced water treatment. Trends Biotechnol 2009;27(2):90–8.
[30] Duran N, Marcato PD, Duran M, Yadav A, Gade A, Rai M. Mechanistic aspects in the biogenic synthesis of extracellular metal nanoparticles by peptides, bacteria, fungi, and plants. Appl Microbiol Biotechnol 2011;90(5):1609–24.
[31] Bansal V, Rautaray D, Ahmad A, Sastry M. Biosynthesis of zirconia nanoparticles using the fungus Fusarium oxysporum. J Mater Chem 2004;14(22):3303–5.
[32] Sanyal A, Rautaray D, Bansal V, Ahmad A, Sastry M. Heavy-metal remediation by a fungus as a means of production of lead and cadmium carbonate crystals. Langmuir 2005;21(16):7220–4.
[33] Bansal V, Rautaray D, Bharde A, Ahire K, Sanyal A, Ahmad A, et al. Fungus-mediated biosynthesis of silica and titania particles. J Mater Chem 2005;15(26):2583–9.
[34] Umashankari J, Inbakandan D, Ajithkumar TT, Balasubramanian T. Mangrove plant, *Rhizophora mucronata* (Lamk, 1804) mediated one pot green synthesis of silver nanoparticles and its antibacterial activity against aquatic pathogens. Aquat Biosyst 2012;8(1):11.
[35] Yong P, Mikheenko IP, Deplanche K, Redwood MD, Macaskie LE. Biorefining of precious metals from wastes: an answer to manufacturing of cheap nanocatalysts for fuel cells and power generation via an integrated biorefinery? Biotechnol Lett 2010;32(12):1821–8.
[36] Mabbett AN, Sanyahumbi D, Yong P, Macaskie LE. Biorecovered precious metals from industrial wastes: single-step conversion of a mixed metal liquid waste to a bioinorganic catalyst with environmental application. Environ Sci Technol 2006;40(3):1015–21.
[37] Gorby YA, Beveridge TJ, Blakemore RP. Characterization of the bacterial magnetosome membrane. J Bacteriol 1988;170(2):834–41.
[38] Naresh M, Das S, Mishra P, Mittal A. The chemical formula of a magnetotactic bacterium. Biotechnol Bioeng 2012;109(5):1205–16.
[39] Gorby YA, Yanina S, McLean JS, Rosso KM, Moyles D, Dohnalkova A, et al. Electrically conductive bacterial nanowires produced by *Shewanella oneidensis* strain MR-1 and other microorganisms. Proc Natl Acad Sci U S A 2006;103(30):11358–63.
[40] Diels L, van Roy S, Somers K, Willems I, Doyen W, Mergeay M, et al. The use of bacteria immobilized in tubular membrane reactors for heavy metal recovery and degradation of chlorinated aromatics. J Membr Sci 1995;100(3):249–58.
[41] Srivastava SK, Constanti M. Room temperature biogenic synthesis of multiple nanoparticles (Ag, Pd, Fe, Rh, Ni, Ru, Pt, Co, and Li) by *Pseudomonas aeruginosa* SM1. J Nanopart Res 2012;14(4).
[42] Tsoi KM, Dai Q, Alman BA, Chan WCW. Are quantum dots toxic? Exploring the discrepancy between cell culture and animal studies. Acc Chem Res 2012;46(3):662–71.
[43] Krug HF, Wick P. Nanotoxicology: an interdisciplinary challenge. Angew Chem Int Ed 2011;50(6):1260–78.
[44] Arkin A. Setting the standard in synthetic biology. Nat Biotechnol 2008;26(7):771–4.
[45] Frow E, Calvert J. 'Can simple biological systems be built from standardized interchangeable parts?' Negotiating biology and engineering in a synthetic biology competition. Eng Stud 2013;5(1):42–58.
[46] Biobrick Foundation Available from: http://biobricks.org/.

Please cite this article in press as: Edmundson, M.C. et al., Exploring the potential of metallic nanoparticles within synthetic biology, New Biotechnol. (2014), http://dx.doi.org/10.1016/j.nbt.2014.03.004