

Astromimetics: The dawn of a new era for (bio)materials science?

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journals.sagepub.com/home/nab**Vuk Uskoković¹** and **Victoria M Wu²**

Abstract

Composite, multifunctional fine particles are likely to be at the frontier of materials science in the foreseeable future. Here we present a submicron composite particle that mimics the stratified structure of the Earth by having a zero-valent iron core, a silicate/silicide mantle, and a thin carbonaceous crust resembling the biosphere and its biotic deposits. Particles were formulated in a stable colloidal form and made to interact with various types of healthy and cancer cells in vitro. A selective anticancer activity was observed, promising from the point of view of the intended use of the particles for tumor targeting across the blood–brain barrier. As an extension of the idea underlying the fabrication of a particle mimicking the planet Earth, we propose a new field of mimetics within materials science: astromimetics. The astromimetic approach in the context of materials science consists of the design of particles after the structure of celestial bodies. With Earth being the most chemically diverse and fertile out of all the astral bodies known, it is anticipated that the great majority of astromimetic material models will fall in the domain of geo-inspired ones.

Keywords

Carbon, cell culture, composite nanoparticle, fluorescence, magnetism, mimicry, nanomedicine, TEM

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The idea that the natural world abounds with materials whose properties are in many respects superior to their synthetic counterparts has given rise to directions of research oriented toward the mimicry of such materials and of the processes leading to them. Although various natural disciplines could yield sources of inspiration to materials scientists, the sole and, naturally, the most prominent of such directions of research has been biomimetics,¹ whose goal is to imitate the biological fabrication processes for the sake of sophisticating the structure and improving the properties of advanced materials. Structural mimicry of the components of the biosphere has yielded numerous advanced materials and concepts, ranging from (i) the photonic nanostructures modeled after the iridescent spine of the sea mouse² to (ii) high aspect ratio apatite fibers that mimic the tooth enamel in fabrication process and structure³ to (iii) composites combining brittle platelets and thin layers of elastic biopolymers that inhibit transverse crack propagation after finding an inspiration in the shell of

marine mollusks⁴ to (iv) surface functionalization of prokaryotic and eukaryotic cells⁵ to mimic the protective coatings posited around more complex organisms, including humans, and beyond. However, the idea that physical structures and relationships need not be literally imitated but taken on as an inspirational analogy, a concept to be translated to another domain, has not been expounded as often.⁶ A new field that we propose on the basis of this concept is that of astromimetics, the core idea of which is that materials science objects, such as particles or thin films, could

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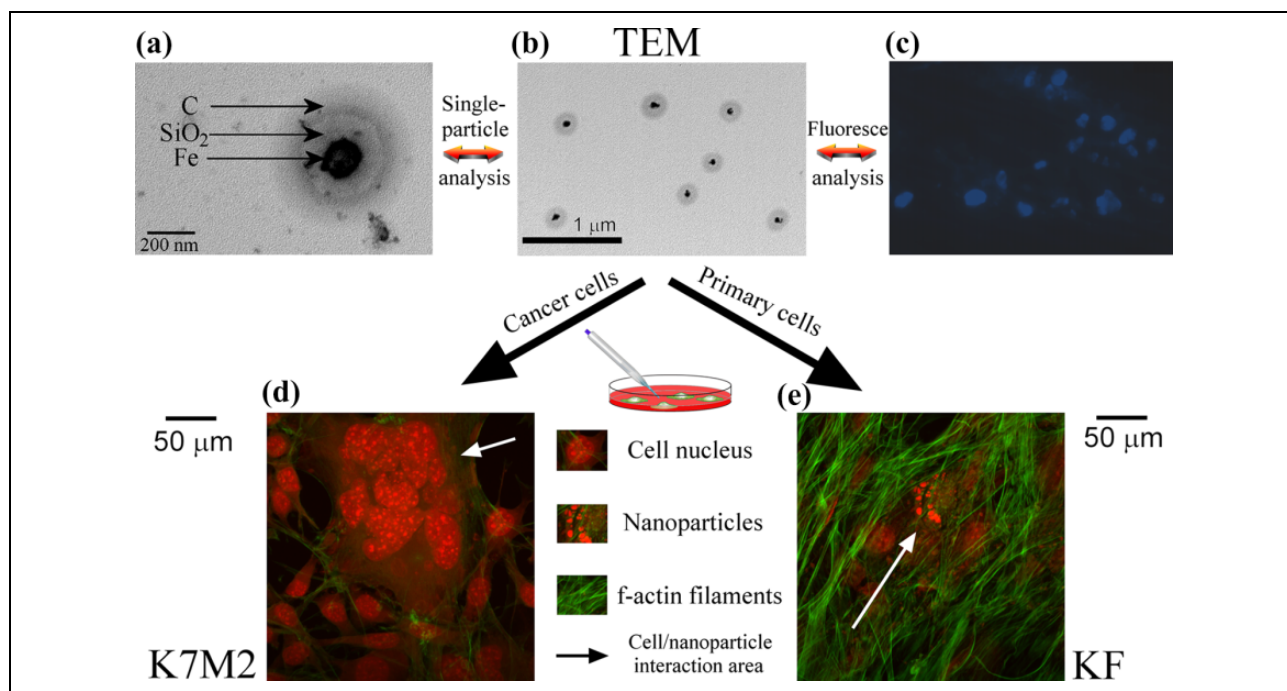


Figure 1. The scheme representing the stratified structure of the “earthicle,” its fluorescence due to the graphitic carbon crust and selective interaction with respective to K7M2 osteosarcoma cancer cells and healthy kidney fibroblasts in an immunofluorescent in vitro cell culture assay. (a) A single “earthicle” observed in a TEM analysis. (b) Multiple iron particles coated with silica/carbon and detected at a lower resolution in a TEM analysis. (c) Fluorescence of the particles in the blue optical range due to the carbon coating after an excitation by the coherent, monochromatic light source at $\lambda = 355$ nm. (d) K7M2 osteosarcoma cells aggregating in a necrotic process due to interaction with the composite particles. (e) Kidney fibroblasts exhibiting healthy F-actin filament patterns, no loss of cell density, and overall showing no signs of toxicity, with some cells internalizing considerable doses of the particles. TEM: transmission electron microscopy; KF: kidney fibroblasts.

be modeled after the forms, structures, and compositions intrinsic to the celestial bodies.

With the planet Earth counted among such bodies, a geomimetic approach could be seen as yet another novel branch of materials science and a subset of the broader field of astromimetics. With humans being literally made of the starry matter and with striking similarities between patterns typifying terrestrial landforms and biological systems,^{7,8} it is conceivable that this new form of mimetics might lead to biomaterials more suitable to replace or augment the defective tissues than their current generation. Moreover, with Earth being the most compositionally and microstructurally diverse and fertile out of all the astral bodies known, it should not be surprising if the great majority of astromimetic models turn out to fall in the domain of geo-inspired ones. One example of an astromimetic/geomimetic material comes from the recently synthesized particle, also known as “earthicle,” containing stratified, core/shell/crust form structurally and compositionally similar to the planet Earth⁹ (Figure 1(a) and (b)). Specifically, as indicated by transmission electron microscopy (TEM) and X-ray mapping, the composite nanoparticles contained a zero-valent iron core, a mixed silica and iron silicate/silicide meso-layer, and an amorphous carbon shell, with a similar ratio between the diameter of the iron core and the thickness of

the silica/carbon shell (1:3.9) as that between the radius of the Earth’s core and the combined thickness of the silicate mantle and the crust (1:4.9). The particles are synthesized using sequential precipitation in reducing atmosphere and controlled pyrolysis of aqueous citrate either through solid-state annealing or, as of recently, in the newest iteration of the method, hydrothermal processing. The particles assume a stable colloidal form and each of the three components potentially endows the particle with a property of medical significance: (a) the magnetic core for external field guiding, magnetic resonance imaging contrast, and/or hyperthermia effect in an alternate magnetic field; (b) the silicate shell dopable with light transducers for upconversion of low-penetrating ultraviolet and X-rays into frequencies activating photosensitizers capable of converting the external electromagnetic radiation into reactive oxygen species, thus enabling the use of the particles in photodynamic therapies; and (c) facily functionalizable carbon exhibiting fluorescent properties that allow for cell imaging, biolabeling, and tracking. Specifically, resulting from the interband $\pi-\pi^*$ transition characteristic of graphitic structures, the composite particles fluoresced in the blue range of the optical spectrum after being excited by the laser light at $\lambda = 355$ nm (Figure 1(c)). This multimodal, synergistic, theranostic form coincides with the composite

nanoparticle as a type of material destined to remain at the frontier of biomedicine for many decades, if not centuries, to come.¹⁰

Made to react with different cell types *in vitro*, the earth-like particles were shown in an immunofluorescent assay to cause the apoptotic rounding and congregation of cells in K7M2 osteosarcoma culture (Figure 1(d)), while eliciting no necessarily negative morphological effects at low concentrations and at the point of contact against the primary kidney fibroblasts (Figure 1(e)). This selective, targeted effect was also noticed in terms of the healthier looking, striated pattern of cytoskeletal F-actin microfilaments in healthy cells as opposed to the cancerous ones. Further tests will focus on assessing the effects of the magnetism and conjugation of chemotherapeutics to sp^2 hybridized carbon as well as optimizing the particles for biological barrier permeability.

However, this is not the sole example of this new form of mimetics in materials science. Arguments were, for example, made in favor of hydrothermal reaction conditions as those that replicate the early Earth's atmosphere and under which products of tremendous potential could be synthesized,¹¹ including the Earth-abundant transition metal nanocatalysts,¹² such as graphitic carbon nitride, a highly efficient and versatile photocatalyst and chemical catalyst.¹³ Replicating the slow ambient sedimentation may also lead to materials with interesting properties, such as the birefringent, laminated, ultrastrained, dendritic, and spongy siliceous deposits around the Yellowstone geysers¹⁴ or the highly enriched banded iron formations of the Mareman Dome,¹⁵ even more so in the forthcoming age of 2-D materials and thin films with precisely tailored atomic layer compositions.^{16,17} Such conditions of growth may also lead to stalactitic halide and other speleothemic, uniaxial water-soluble morphologies that may prove to be more benevolent for drug delivery across epithelial and endothelial monolayers than their insoluble counterparts.¹⁸ Simulating more dynamic geologic phase transitions, such as those occurring in geothermal pools or deep-sea vents, where the crystal formation is the result of abrupt drops in hydrothermal pressures and rapid cooling of high-temperature fluids, may lead to equally attractive structures.¹⁹ Mimicking magmatic solidification conditions can be one such route to exciting materials, one example of which is pure anorthosite formed upon the cooling of the lunar sea and constituting the light-colored regions of the Moon's surface.²⁰ Next, subjecting laboratory models of the Earth to ultrahigh pressures on nanosecond timescales modified the crystal structure of the iron core from the hexagonal close-packed to body-centered cubic as the size of the model increased and entered the region of super-Earths.²¹ By knowing that this iron core symmetry affects not only the magnetic field of the planet but also its thermal evolution, mass-radius relation, tectonic movements, seismic profiles, and multiple other physical properties that may or may not be conducive to the unfolding of life on

it, an endless room opens for exploring the particle properties resulting from such experimentations with the magnetic core of the particle in settings that simulate Earth-like planets on the laboratory scale.

Because the mimicry process here need not be literal, but can feed on the imitation of a concept, the possibilities toward tweaking the systems toward desired applications are more open to imagination rather than sole rigor, as is the common case with biomimetics. For example, the particle structure modeled after the planet Earth—although literally impossible to achieve because of the ultrahigh pressures needed to preserve the Fe/Ni core in the liquid state—can have infinite compositional variations; for example, in place of the amorphous carbon coating there could be graphene, carbide, and/or nitride monolayers, different covalently functionalized polymeric shells, a rigged calcite crust that would resemble continents, and so on. It has been known for decades now that not uniformization, but correct distribution of charges, topologies, and lipophilic pockets on a curved particle surface, as is the case with proteins and other biomolecules, is the key to producing a desirable therapeutic effect at the target.²² Therefore, the modeling of the particle surface after the diverse face of the Earth, with distinct regions occupied by oceans, continents, deserts, and cyclones, may be the way to endow an exogenous particle with the therapeutic efficacy of endogenous biomolecular species. Other celestial bodies could be used as models with similar flexibility: comet-like structures if “missiles” for targeted drug delivery are intended, asteroids if trojans or protective belts around functional particles are desired, Mercury as a mantle-free iron-core planet to avoid the diamagnetic contribution of silica, extrasolar planets to explore spherical composite particle structures different from the Earth's and other rocky solar planets', and so on.

Finally, any product of such astromimetic biomaterials design is bound to be comparatively complex for today's clinical standards. Yet diseases such as cardiovascular, autoimmune, and neoplastic are complex, and it is conceivable that they could be effectively treated solely using equally complex, multimodal agents. However, the problems of irreproducibility in fabrication and clinical outcome are bound to be an inevitable accompaniment of this structural complexity. In addition to the cost, especially in the stage before the technology matures, these can be the sources of significant regulatory hurdles.²³ For example, in analogy with combination drug therapies, the use of novel components in a composite biomaterial would require the Food and Drug Administration (FDA) approval for each of them separately, which is a standard practice in use for medical devices, but which renders such clinical trials potentially unethical in case a positive outcome is expected only from their synergistic combination.²⁴ This is the main reason why at the moment the exceptionally simple biomimetic entities, such as liposomes, represent the gold standards for nanomedical applications. However, just as small ions have a limited therapeutic potential compared to larger

molecular species in systems built and sustained by complex molecules,²⁵ so are the prospects of simple particle compositions and structures questionable in the treatment of complex, multivariable diseases, even though they may be more economic, elegant, and easy to apply, alongside being more industrially scalable, more accessible, and on a smoother regulatory approval path.^{26,27} This antagonism between simplicity and complexity in the design of nanoparticles for biomedical applications will continue to perplex the scientists in the decades and centuries to come. As for now, a balance is called to be stricken by designing particles that may comprise simpler components, which, when combined, create a sophisticated complexity that can tackle the issues produced by multivariate disease processes. The Earth with its endless geochemical complexities is at its rock bottom a solid composite of mineral compounds predominantly based on iron, oxygen, and silicon, which in their synergy with the solar energies create conditions for the rise of the magnificent phenomenon called life. If an inanimate particle modeled after the Earth could similarly yield life on its surface, what is more to expect from one such concept? To that end, we believe that astromimetics may pave way for a new wave and a new dawn in (bio)materials science. Perhaps time has come to look up at the starry sky or deep inside the Earth for new sources of inspiration in materials design.

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References

1. Frishberg M and Gobble MM. What would nature do? The rise of biomimicry. *Res Tech Manag* 2015; 58: 7–8.
2. McPhedran RC, Nicorovici NA, McKenzie DR, et al. The sea mouse and the photonic crystal. *Aust J Chem* 2001; 54: 241–244.
3. Uskoković V, Li W and Habelitz S. Biomimetic precipitation of uniaxially grown calcium phosphate crystals from full-length human amelogenin sols. *J Bionic Eng* 2011; 8(2): 114–121.
4. Espinosa HD, Juster AL, Latourte FJ, et al. Tablet-level origin of toughening in abalone shells and translation to synthetic composite materials. *Nature Comm* 2011; 2: 173.
5. Naumenko EA, Dzamukova MR, Fakhrullina GI, et al. Nano-labeled cells—a functional tool in biomedical applications. *Curr Opin Pharmacol* 2018; 18: 84–90.
6. Uskoković V. Prospects and pits on the path of biomimetics: the case of tooth enamel. *J Biomim Biomater Tissue Eng* 2010; 8: 45–78.
7. Smolyar I, Bromage T and Wikelski M. Quantification of layered patterns with structural anisotropy: a comparison of biological and geological systems. *Heliyon* 2016; 2(3): e00079.
8. Ball P. Forging patterns and making waves from biology to geology. *Philos Trans Royal Soc B* 2015; 370(1666): 1–10.
9. Uskoković V, Pernal S and Wu VM. Earthicle: the design of a conceptually new type of particle. *ACS Appl Mater Interfaces* 2017; 9(2): 1305–1321.
10. Uskoković V. When $1 + 1 > 2$: nanostructured composite materials for hard tissue engineering applications. *Mat Sci Eng C Mater Bio Appl* 2015; 57: 434–451.
11. Kopetzki D and Antonietti M. Hydrothermal formose reaction. *New J Chem* 2011; 35: 1787–1794.
12. Wang D and Astruc D. The recent development of efficient Earth-abundant transition-metal nanocatalysts. *Chem Soc Rev* 2017; 46(3): 816–854.
13. Wang Y, Wang X and Antonietti M. Polymeric graphitic carbon nitride as a heterogeneous organocatalyst: from photochemistry to multipurpose catalysis to sustainable chemistry. *Angew Chem Int Ed* 2012; 51: 68–89.
14. Lowe DR and Braunstein D. Microstructure of high-temperature ($>73^{\circ}\text{C}$) siliceous sinter deposited around hot springs and geysers, Yellowstone National Park: the role of biological and abiological processes in sedimentation. *Can J Earth Sci* 2003; 40(11): 1611–1642.
15. Klemm DD. The formation of Palaeoprotozoic banded iron formations and their associated Fe and Mn deposits, with reference to the Griqualand West deposits, South Africa. *J Afr Earth Sci* 2000; 30: 1–24.
16. Anasori B, Lukatskaya MR and Gogotsi Y. 2D metal carbides and nitrides (MXenes) for energy storage. *Nature Rev Mat* 2017; 2(2): 16098.
17. Božović I and Ahn C. A new frontier for superconductivity. *Nature Physics* 2014; 10: 892–895.
18. Uskoković V, Lee K, Lee PP, et al. Shape effect in the design of nanowire-coated microparticles as epithelial drug delivery devices. *ACS Nano* 2012; 6(9): 7832–7841.
19. Tobler DJ and Benning LG. In situ and time resolved nucleation and growth of silica nanoparticles forming under simulated geothermal conditions. *Geochim Cosmochim Acta* 2013; 114: 156–168.
20. Piskorz D and Stevenson DJ. The formation of pure anorthosite on the Moon. *Icarus* 2014; 239: 238–243.
21. Wicks JK, Smith RF, Fratanduno DE, et al. Crystal structure and equation of state of Fe-Si alloys at super-Earth core conditions. *Sci Adv* 2018; 4(4): eaao5864.

22. Seelig A, Gottschlich R and Devant RM. A method to determine the ability of drugs to diffuse through the blood-brain barrier. *Proc Natl Acad Sci USA* 1994; 91(1): 68–72.
23. Heidt T and Nahrendorf M. Multimodal iron oxide nanoparticles for hybrid biomedical imaging. *NMR Biomed* 2013; 26(7): 756–765.
24. Woodcock J, Griffin JP and Behrman RE. Development of novel combination therapies. *New Eng J Med* 2011; 364(11): 985–987.
25. Uskoković V, Iyer MA and Wu VM. One ion to rule them all: the combined antibacterial, osteoinductive and anticancer properties of selenite-incorporated hydroxyapatite. *J Mat Chem B* 2017; 5(7): 1430–1445.
26. Wolf LK. Personalizing nanomedicine. *Chem Eng News* 2011; 89(39): 29–32.
27. Uskoković V and Wu VM. Calcium phosphate as a key material for socially responsible tissue engineering. *Materials* 2016; 9(6): 434–460.