



## Editorial

## Special issue on “Ultrasound-assisted engineering of materials for biomedical uses”



To highlight the emerging use of ultrasound for engineering new nanomaterials for biomedical uses, including drug delivery and biosensing systems and nutraceutical agents, a special issue was arranged, which has 11 published papers on important concepts in this field moving forward.

Delivering drugs to specific cancer tissue has long been, and remains, a challenge in the field of bio-nanomedicine. In this pursuit, encapsulation of therapeutic drugs in vehicles for specific uptake and/or release at a target is a promising strategy. Bhargawa et al. [1] have reported on the development of lysozyme microspheres with embedded gold nanorods as a basis for the ultrasound-mediated release of a model drug 5-Fluorouracil. The microspheres were about 4  $\mu\text{m}$  in diameter, and after exposure to 200 kHz ultrasound, the microspheres burst, releasing the encapsulated drug. The authors showed this resulted in 97 % cell death against THP-1 cells, which shows great promise for the use of ultrasound-mediated drug release.

Vidallon et al. [2] have reported on the ultrasound-assisted fabrication of polydopamine-shelled perfluorocarbon emulsion droplets, which were used as photoacoustic signal enhancers using tissue-mimicking phantoms. The authors surveyed different parameters for controlling size distributions, where different phantoms could be designed (optical scattering and absorption of tissues), which highlights the potential of the system for predicting the in vivo efficiency of colloidal photoacoustic imaging agents.

The successful delivery of small interfering RNA (siRNA) is pivotal for its use as a treatment for numerous diseases, where the stability of the siRNA is an issue. Cortez-Jugo et al. [3] reported on the nebulisation of siRNA solutions using a miniaturizable acousto-microfluidic nebulization device. This device produced complexes about 3  $\mu\text{m}$ , as appropriate for deep lung deposition via inhalation. The material was tested for its stability and gene silencing capabilities, where it was found the properties were retained after nebulization. The work highlights the potential for fast and effective delivery of siRNA via inhalation.

Transforming small-molecule antibiotics into carrier-free nanoantibiotics represents an opportunity for developing new multifunctional therapeutic agents. Zhu et al. [4] introduced a strategy for fabricating carrier-free doxycycline nanodrugs using high frequency ultrasound. The morphology of obtained particles could be finely controlled by tuning the applied ultrasonic powers. The sono-assembled nanodrugs exhibit excellent antioxidant properties, along with antimicrobial activity against both Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) bacteria.

Sonodynamic therapy (SDT) employs ultrasound transducers and sonosensitizers to generate reactive oxygen species ROS, is highly effective in killing bacteria and for the treatment of deep infections. A

new nanosensitizer (HFH@ZIF-8) for sonodynamic therapy was engineered by Geng et al. [5] for killing multidrug-resistant bacteria and treatment of in vivo infection diseases. The nanosensitizer is obtained by combining oxygen-carrying hematoporphyrin monomethyl ether and zeolitic imidazolate framework-8. The developed HFH@ZIF-8 exhibited enhanced water-solubility, good biocompatibility and ROS generating efficiency, as well as disease-targeting capability.

Flow-through ultrasonication method was used by Hashad et al. [6] to produce spherical and uniformly dispersed nisin-shelled nanovesicles with long term stability, low toxicity and able to accommodate a high concentration of anticancer drugs and augment their cytotoxic effect. The nisin shelled nanovesicles were exploited for the site-specific attachment of a recombinantly produced cancer targeting ligand ( $\alpha\text{HER2LPETG}$  IgG) and showed cancer-specific binding and augmented cytotoxicity to HER2 expressing tumour cells. Biological assays proved that nisin was assembled at the water–oil interface in a way where the antibacterial binding region (AB ring fragment) in nisin structure and the lysine residue 12 are directed outwards in the aqueous phase and are exposed for surface reactions. Therefore, the combined bactericidal/cytotoxic effect of NSNE when loaded with a cytotoxic drug paves the way for a dual therapy platform for bacterial infections in cancer patients.

Usen et al. [7] have reported on the sonochemical synthesis of porous gold particles in a Rosette cell. This process relied on the reducing capability of  $\alpha\text{-D}$ -glucose under 20 kHz ultrasound irradiation. The particle size, morphology, and porosity could be tuned by varying synthesis parameters, and thereby establishes a new and low-cost method for the synthesis of gold nano-to-microparticle structures for use in biomedical applications.

Ultrasonic assisted extraction is a non-conventional extraction technique that does not require thermal treatments and large solvent volumes. Non-invasive biomedical benefits of ultrasound-assisted extraction of compounds from various food sources is reviewed and critically discussed by Mounika et al. [8] The review provides a comprehensive description of several bioactive compounds that can be extracted from different natural sources (propoli, pomegranate and orange peels, grape skins, mango pomace, raspberries, purple basil etc) using ultrasound with high efficacy and various biomedical properties (cardiovascular, anti-diabetic, antiobesity antioxidant anti-cancer and antimicrobial properties). On this note, Shokri et al. [9] have reported on the effect of ultrasound on the physical and chemical properties of milk proteins. The results showed that the improving effects of ultrasound on the functional properties of milk proteins is entirely dependent on the ultrasound treatment conditions and the type of ultra-sonicated protein.

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Detection of acetone is important of monitoring the rates of lipolysis in obese patients. Cho et al. [10] have reported on the development of cobalt-doped zinc oxide microbeads (~500 nm in diameter) synthesised using sonochemical processes for use as diagnostic devices for the detection of acetone. The materials could detect acetone down to 43 ppb. The materials were found to be sensitive due to the catalytic role of  $\text{Co}^{3+}$  on acetone oxidation. These were used to monitor the acetone concentration in 1 mL of exhaled air from a healthy adult, revealing a concentration of 0.44 ppm.

In biological sciences, nucleobase analysis is crucial, particularly in the diagnosis of infectious illnesses and the research of genetic alterations. Gold-loaded boron-doped graphene quantum dots were prepared via ultrasound-aided reduction method for monitoring guanine and adenine electrochemically by Kaimal et al. [11] The nanocomposite sensor exhibited high electrocatalytic activity, stability a good response with a wide linear range, a low detection limit, excellent sensitivity, and good repeatability.

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**Dr. Quinn A. Besford** received his PhD in chemistry from The University of Melbourne. He is currently a Group Leader at the Leibniz Institute for Polymer Research in Dresden, Germany, and lecturer on the application of nanomaterial systems in biomedicine at the Technical University of Dresden. His research team focuses on developing functional polymer architectures for mechanosensing and theranostic applications. Of particular interest is developing biocompatible and biodegradable nanomaterial systems, focused on in-blood interactions and targeting. Dr. Besford transitioned to Germany in 2019 as an Alexander von Humboldt research fellow (Ludwig Leichhardt Memorial Fellowship), following a postdoctoral position at The University of Melbourne (2016–2018). Dr. Besford's research has attracted multiple sources of funding from within Germany and internationally, and he has presented his work at numerous conferences as an invited speaker. He has published more than 40 peer-reviewed publications (830 citations, *h*-index 16).



**Dr. Francesca Cavaliere** received her Laurea degree, '*maxima cum laude*,' in Industrial Chemistry from the University of Rome La Sapienza and PhD in Chemistry at the University of Melbourne. She is an Associate Professor at RMIT University in Melbourne, (Australia) and Senior Lecturer at the University of Rome 'Tor Vergata'. She was awarded the Australian Research Council Future Fellowship in 2015 and Vice Chancellor Senior Research Fellowship at RMIT University in 2019. Dr Cavaliere has a broad expertise in the synthesis and structural-biological characterization of nanostructured materials based on biomacromolecules (polysaccharides, proteins, nucleic acids) for gene and drug delivery applications. In the last fifteen years she also expanded her research interest in sonochemistry, owing to its potential to achieve one-pot and mild reactive processing of biomolecules. She has attracted significant national and international research funding, published more than 120 peer-reviewed articles, (4300 citations, *h*-index 35).

Quinn A. Besford  
*Leibniz-Institut für Polymerforschung Dresden e.V., Hohe Str. 6, 01069 Dresden, Germany*

Francesca Cavaliere\*  
*RMIT University, School of Science, RMIT University, Melbourne, VIC, 3000, Australia*

\* Corresponding author.